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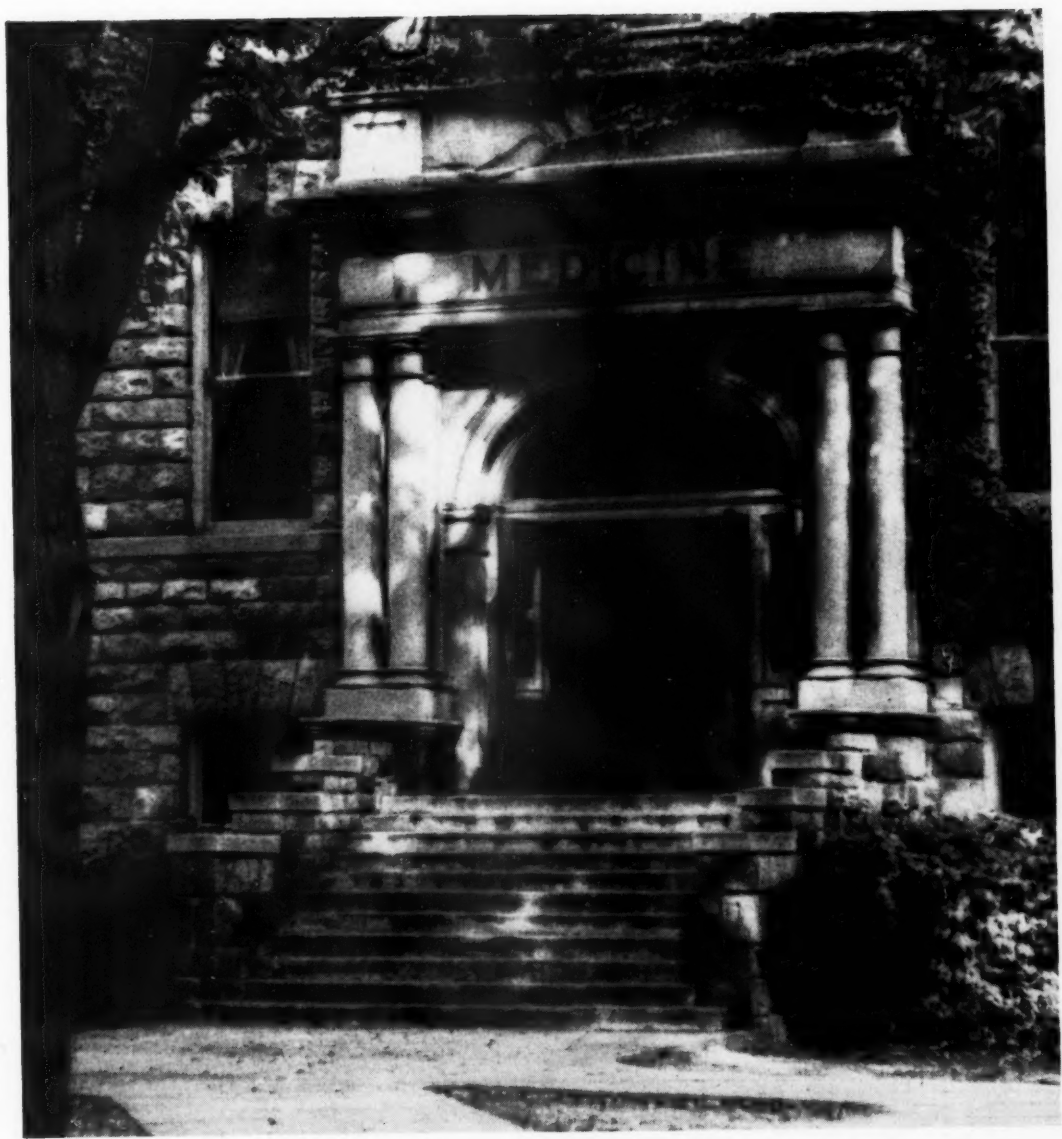
# the JOURNAL

## MICHIGAN STATE MEDICAL SOCIETY

Volume 46

Number 5

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*"Through these portals . . ."*

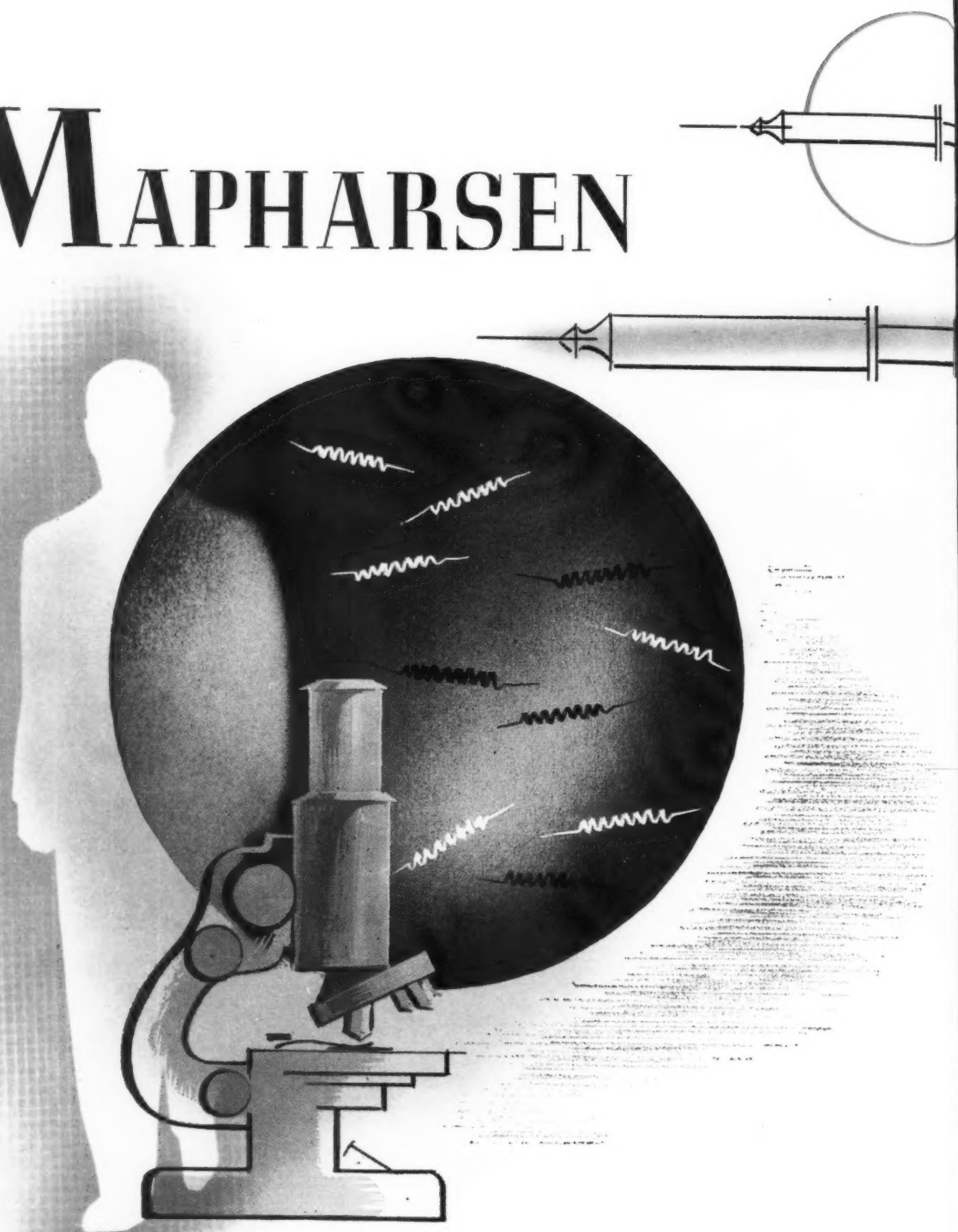
University of Michigan  
Medical School,  
Ann Arbor, Michigan

**MAY, 1947**

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SYMBOLS OF SIGNIFICANCE

# MAPHARSEN





### 3 "Premarin" tangibles... plus

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**"Premarin"** is well tolerated

**"Premarin"** provides rapid symptomatic relief

... and as a sequel to the control of subjective symptoms, there is the emotional uplift or feeling of well-being which is so frequently reported by patients on "Premarin" therapy. "Premarin" has proved to be a valuable therapeutic medium for the management of the menopause and other manifestations of estrogenic deficiency.

To permit flexibility of dosage and enable the physician to fit estrogenic therapy to the particular needs of the patient, "Premarin" is supplied in two potencies — tablets of 1.25 mg. and 0.625 mg. Also available in liquid form, containing 0.625 mg. in each 4 cc. (1 teaspoonful).

\*Although the principal estrogen in "Premarin" is sodium estrone sulfate, it also contains other equine estrogens . . . estradiol, equilin, equilinenin, hippulin . . . which are also present as water soluble sulfates. The water solubility of conjugated estrogens (equine) assures rapid absorption from the gastrointestinal tract.



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# You and Your Business

## WILL YOUR NAME BE IN THE MSMS ROSTER?

The Roster Number of *THE JOURNAL* (July, 1947) will go to press June 10.

The Roster will include the names of all physicians, members of the Michigan State Medical Society, with 1947 dues and assessments paid on or before June 10.

Be sure your name is in the Directory Number. If you have not already done so, contact the Secretary of your County Medical Society today.

\* \* \*

## INCREASE IN V.A. HOSPITALS

During 1946, *Veterans Administration* increased the number of its hospitals from 97 to 122. This represents a 23 per cent increase in beds available, from 79,450 to 97,772. V.A. reports a total of 458,749 admissions of veteran-patients to V.A. and non-V.A. hospitals during 1946, an increase of 61.3 per cent over 1945. The greatest number of admissions (83 per cent of the total) were general medical and surgical patients. V.A. expects to operate more than 200 hospitals, eventually, in order to handle the anticipated load of veteran-patients.

\* \* \*

## BENIGN AND MALIGNANT TUMORS

R. S. Sykes, D.D.S., of Muir, Michigan, has contributed \$500 to the Michigan State Medical Society "to be used for instruction of doctors in the difference between non-pathological swellings and true sarcoma or cancer."

The Michigan State Medical Society has accepted Dr. Sykes' generous gift and has instructed that the fund be used during a five-year period to provide a lecturer at the Annual Session of the Michigan State Medical Society as well as at the Michigan Postgraduate Clinical Institute to speak on the subject "The Differential Diagnosis of Benign and Malignant Tumors."

\* \* \*

## MICHIGAN MEDICAL SERVICE

Taking a new approach toward explanation of Michigan Medical Service, its aims and its veterans' care program, officials of MMS entertained

"the person who sees the patient first" at a luncheon April 15 at the Pantlind Hotel in Grand Rapids.

One hundred thirty doctors' nurses or secretaries, representing 150 Grand Rapids physicians, attended the luncheon and heard Jay C. Ketchum, executive vice president of Michigan Medical Service, trace the operation of MMS since its beginning in 1939 and outline the purposes of the organization.

Gordon Goodrich, assistant director of MMS, explained the veterans' care program, pointing out the necessity for the doctor always to "have prior authorization from the Veterans Administration before the veteran is treated or examined except in extreme emergencies."

An explanation of Michigan Hospital Service, companion organization to Michigan Medical Service, was given by James Foster, manager of MMS district offices.

William A. Hyland, M.D., president of the Michigan State Medical Society, welcomed the guests on behalf of the MSMS, and Kenneth Trim, MMS field representative, acted as toastmaster for the occasion.

\* \* \*

## SPECIAL MEMBERSHIPS IN MSMS

The MSMS House of Delegates, in September, 1946, adopted a resolution instructing that a Committee of the House of Delegates be appointed to handle all recommendations for special memberships. It instructed that such resolutions be given the Chairman of this Committee prior to the first meeting of the Annual Session of the House of Delegates, for presentation *in toto* by the Chairman to the House of Delegates, to conserve the time of the House.

Delegates from the various county medical societies are requested, therefore, to refer all recommendations for Emeritus, Retired, Honorary, Associate, et cetera, memberships to the Secretary of the House of Delegates who in turn will present same, *in toto*, to the Chairman of the Special Committee on Special Memberships.

(Continued on Page 502)



# to convert the diabetic into a more normal person



"The ideal in therapy... is to convert the diabetic into a normal person."<sup>1</sup> While certain restrictions must always be imposed, many patients can be controlled through diet alone so as to dislocate their normal habits as little as possible. In those cases where insulin therapy is also required, control may often be attained with but *one daily injection* of 'Wellcome' Globin Insulin with Zinc. Its intermediate action is adaptable to the needs of most mild and many moderately severe cases and adequate control can usually be achieved in three clear-cut steps:

1. *Stabilize the patient* as well as possible on a diet of the desired caloric content. Give a single dose of 15 or 20 units of 'Wellcome' Globin Insulin 30 minutes or more before breakfast.
2. *Adjustment to 24-hour control:* Gradually adjust the Globin Insulin dosage to provide 24-hour control as evidenced by a fasting blood sugar level of less than 150 mgm. or sugar-free urine in the fasting sample.
3. *Adjustment of diet:* Simultaneously adjust the carbohydrate distribution of the diet to balance insulin activity. Initially this may be 2/10 (breakfast), 4/10 (lunch), and 4/10

(supper). Any tendency toward mid-afternoon hypoglycemia may usually be offset by giving 10 to 20 grams of carbohydrate between 3 and 4 p.m. The final adjustment of carbohydrate distribution may be based on fractional urinalyses.

Systematic attention to these details will make possible adequate control of most mild and many moderately severe cases of diabetes with a *single daily injection* of 'Wellcome' Globin Insulin with Zinc.

'Wellcome' Globin Insulin with Zinc is a clear solution, comparable to regular insulin in its freedom from allergenic properties. Available in 40 and 80 units per cc., vials of 10 cc. Accepted by the Council on Pharmacy and Chemistry, American Medical Association. Developed in The Wellcome Research Laboratories, Tuckahoe, New York. U.S. Patent No. 2,161,198. LITERATURE ON REQUEST.

<sup>1</sup>'Wellcome' Trademark Registered

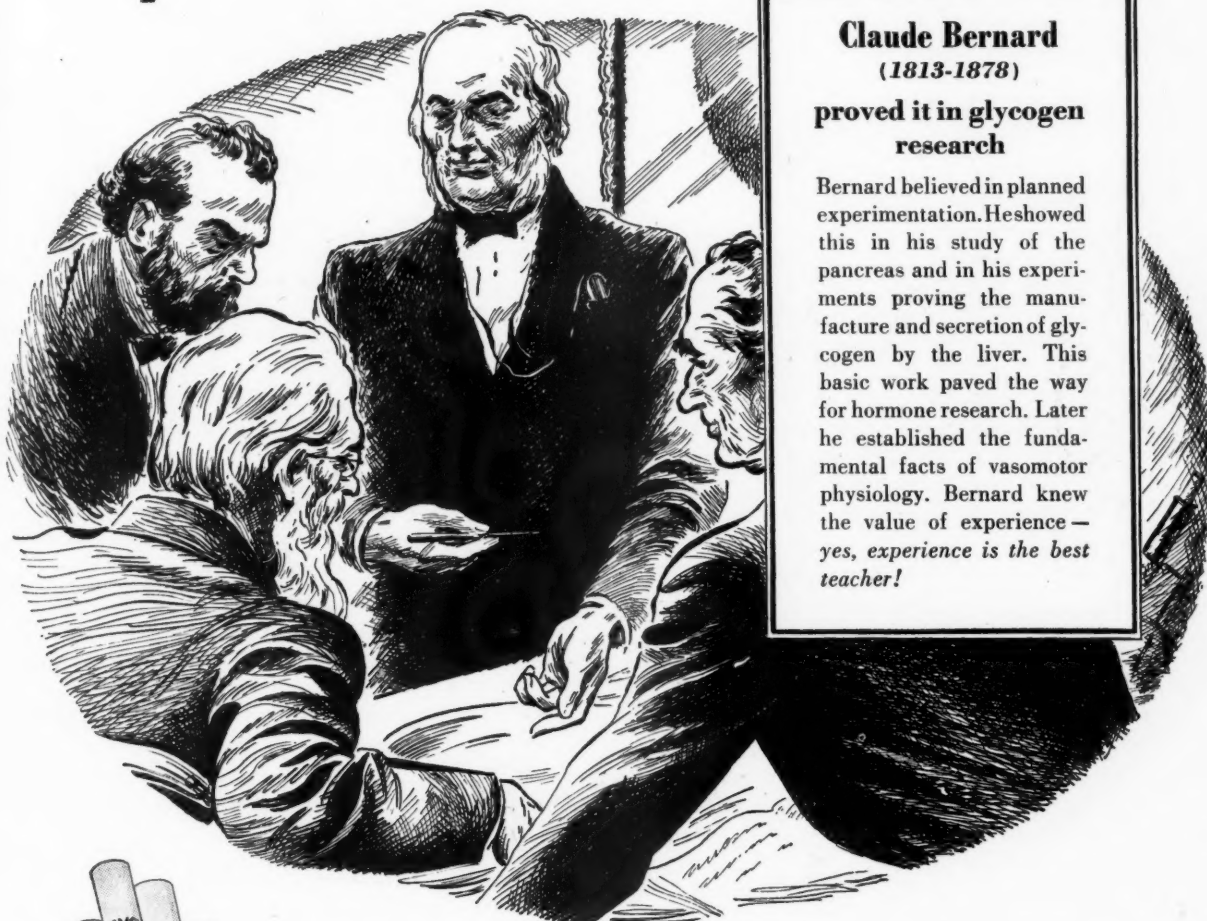
I. Bauman, L.: Bull. New Eng. M. Center 5:17 (Feb.) 1943.



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# Experience is the Best Teacher



## Claude Bernard

(1813-1878)

**proved it in glycogen research**

Bernard believed in planned experimentation. He showed this in his study of the pancreas and in his experiments proving the manufacture and secretion of glycogen by the liver. This basic work paved the way for hormone research. Later he established the fundamental facts of vasomotor physiology. Bernard knew the value of experience — yes, *experience is the best teacher!*



**Yes, and experience is the best teacher in smoking too!**



**T**HAT wartime cigarette shortage was a real experience to smokers. Millions of people smoked more different brands than they would normally try in a lifetime. And out of the comparisons of that experience so many more smokers came to prefer Camels that today more people are smoking Camels than ever before.

***We don't tamper with Camel quality. Only choice tobaccos, properly aged, and blended in the time-honored Camel way, are used in Camels.***

*According to a recent Nationwide survey:*

## MORE DOCTORS SMOKE CAMELS

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MAY, 1947

Say you saw it in the *Journal of the Michigan State Medical Society*

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# National Health Act of 1947

## Senate Bill 545

Summary Prepared by C. Rufus Rorem, Executive Secretary,  
Hospital Council of Philadelphia,  
Philadelphia, Pennsylvania

This Bill was introduced by Senator Robert A. Taft (for himself, Mr. Ball, Mr. Donnell, and Mr. Smith), February 10, 1947, and has been referred to the Committee on Labor and Public Welfare.

### I. Introduction

- A. The Act is cited as the "National Health Act of 1947" (Section 1)
- B. *Preliminary Statement* (Section 2)
  - 1. The bill calls attention to : (a) the *widely scattered* health and medical functions through the many agencies of the federal government; (b) the *inadequacies* of public health and medical and dental *services* in the United States.
  - 2. The bill declares that it is the established policy of the United States:
    - (a) *to aid the various states* through consulting services and grants-in-aid to make available medical, hospital, dental, and public health services to every individual, regardless of race, creed, or color.
    - (b) *"to make provision for voluntary deductions from the salary of Federal employes of premiums directed by them to be paid to voluntary, non-profit health insurance funds."*

### II. National Health Agency (Title I)

- A. *The Agency and the Administrator* (Section 101)

There is established a new and independent *National Health Agency*, to be administered by a full-time *National Health Administrator* to be appointed by the President at a salary of \$15,000 per annum. The Administrator must be a licensed doctor of medicine "who is outstanding in the field of medicine."
- B. *Purpose of the Agency* (Section 102)

To promote the general welfare by aiding and fostering progress in the field of health and centralizing all Federal government agencies concerned with health.
- C. *Duties of the Agency* (Section 102)
  - 1. To encourage the development of health services and facilities
  - 2. To co-operate with federal, state and private agencies

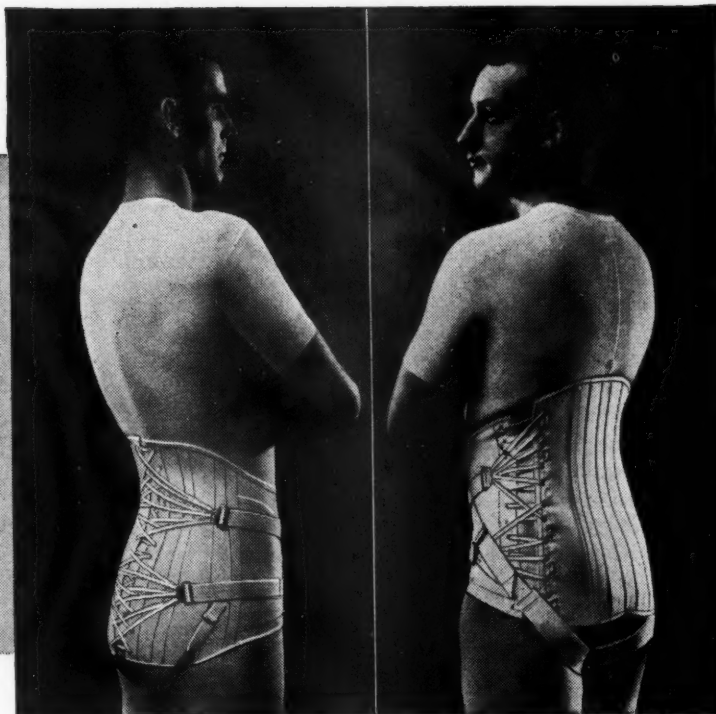
There have been several analyses of the S. 545, one by the A.M.A., another in our editorial in April, and this one by Mr. Rorem. This is complete and concise, and we are glad to give it space for the information of our readers.

- 3. To collect and analyze statistics, etc.
- 4. To make studies of policies and methods
- 5. To perform other specific duties as directed by the Congress
- D. *Responsibility for Federal Government Activities* (Section 102)
  - 1. *Administration of funds* appropriated as grants-in-aid to the states *for medical, dental and hospital care*, hospital facilities, etc.
  - 2. *Administration of Hospital Survey and Construction Act* (Public Law 725)
  - 3. Prevention of disease through various public health activities in the field of sanitation
  - 4. Promotion of maternal, prenatal and child care
  - 5. Regulation of food, drugs and cosmetics
  - 6. Training and rehabilitation of vocationally handicapped persons
  - 7. Handling of other matters pertaining to the national health
- E. *Duties Transferred from other Federal Agencies* (Section 103)
  - 1. No activities in the field of health would be transferred from the Army, Navy or Veterans Administration.
  - 2. The Agency would take over the duties, personnel, funds, properties and records of:
    - (a) The Federal hospitals in Washington, D. C.
    - (b) The Food and Drug Administration
    - (c) The Children's Bureau
    - (d) The Division of Health Studies in the Bureau of Research and Statistics of the Social Security Administration
- F. *Organization of the Agency* (Section 104)
  - 1. *The Agency will be composed of the following units:*
    - (a) Office of the Administrator
    - (b) The Public Health Service (Surgeon General)
    - (c) Office of Medical and Hospital Care (Director an M.D.)
    - (d) Office of Dental Care Services (Director a D.D.S.)
    - (e) The Office of Maternal and Child Health
    - (f) The Office of Health Statistics
    - (g) The Food and Drug Administration
    - (h) Others as deemed necessary
  - 2. *Appointment of executive officers*
    - (a) Details of the Food and Drug Administration remain unchanged

(Continued on Page 506)



**FIGURE 1** — Patient — thin type of build with beginning faulty body mechanics. The Camp adjustment provides a more stable pelvis, allowing patient to "draw in" the abdominal muscles thus gradually acquiring a gentle lumbar curve.



**FIGURE 2** — Patient — intermediate type of build. Strain of lumbosacral joint predisposes to other strains. For protection of the joints in the lumbar region from recurrent strain and also as an aid in relieving the pain of acute conditions, Camp lumbosacral supports have proved effective.

## *In the Conservative Treatment of* The Lumbosacral and Lower Lumbar Regions

### **CAMP** SUPPORTS offer advantages

- ...Give firm support to the low back; the support is easily intensified by re-inforcement with pliable steels or the Camp Spinal Brace.
- ...Afford a more stable pelvis to receive the superincumbent load.
- ...Allow freedom for contraction of abdominal muscles under the support in instances of increased lumbar curve (fig. 1).
- ...Are removed easily for prescribed exercises and other physical procedures prescribed by physiatrist or physician.

**S. H. CAMP AND COMPANY • JACKSON, MICHIGAN**

*World's Largest Manufacturers of Scientific Supports*

Offices in New York • Chicago • Windsor, Ontario • London, England



## NATIONAL HEALTH ACT OF 1947

(Continued from Page 504)

- (b) The Surgeon General of the Public Health Service will continue to be appointed by the President.
  - (c) Other heads of the constituent units are to be appointed by the "Administrator."
  - (d) The head of the Office of Maternal and Child Health Services (qualifications not stated) shall be assisted by an Advisory Council of eight persons (appointed by the administrator) three of whom shall be physicians who are specialists in obstetrics or pediatrics.
3. The Administrator is directed to make a *study of the organization* and staff of the Agency, and to make recommendations within six months on such matters as salaries, the commissioned corps of the Public Health Service, and the desirability of establishing an Office of Health and Medical Research.

### III. Special Cancer Appropriation (Section 203)

\$10,000,000 is provided to enable the Surgeon General to develop a program for prevention and control of Cancer through grants-in-aid and other methods in co-operation with state and local government health agencies.

### IV. General Medical Service for Families and Individuals of Low Incomes (Title VII)

#### A. Medical Care Survey (Section 701-703)

\$3,000,000 is authorized for grants-in-aid to States for surveys of medical and hospital care needs, to be allotted on a matching basis (\$1.00 federal for \$2.00 state) to States according to population, up to the total appropriation. Minimum per State is \$10.00.

The requirements to qualify for survey grants-in-aid, are essentially the same as outlined in Section 712.

#### B. Medical Care Services

##### 1. Appropriations (Section 711)

An annual appropriation of \$200,000,000 is provided for five years, to assist the states to *provide general health, hospital and medical services for families and individuals with low incomes*. The sums appropriated will be used for making payments to the states which have submitted "Plans and had them approved by the Director of Medical and Hospital Care Service."

##### 2. Standards for a State plan which may qualify for grants-in-aid (Section 712)

- (a) Designation of a *single state agency* to handle the program.
- (b) Designation by the Governor of a *State medical and hospital care advisory council* which will include representatives of nongovernment and state agencies concerned with the administration or utilization of health or medical services.

(c) *Satisfactory evidence of authority*.

(d) The program must be calculated to provide (within 5 years)

- (1) *hospital, surgical and medical services in hospitals, clinics, or similar institutions* for all those families and individuals in the state having insufficient income to pay the whole cost of such service.
- (2) *periodic physical examinations* for all children in elementary or secondary schools in the state.

(Approved hospital, surgical and medical service programs may provide for furnishing care to families and individuals through *payments by the State to non-profit voluntary health, medical or hospital insurance funds*, "as premiums, partial premiums, reimbursement of expenses, or otherwise."

*State payments may be made directly to local government or voluntary non-profit health programs, also to physicians practicing in areas which, without such payments, would be unable to provide sufficient income to attract a practicing physician).*

(e) *Financial participation* by the State.

(f) Statement of the priority of various proposals in the plan.

(g) Completion of a state-wide inventory of health facilities.

(h) Provision for reports and periodic review.

##### 3. Basis of Grants-in-Aid (Section 713)

There would be varying ratios of grants-in-aid by the Federal government (based on each State's population and tax-paying ability) not to exceed two-thirds or to be less than one-fourth of the total expenditures by a State plan. Agencies administering the State plans will submit complete reports to the Director. There is provision for appeals which may be made with respect to rulings and regulations.

##### 4. National Medical Care Council (Section 715)

This is an advisory body with whom the Director shall "consult" in administering the Medical and Hospital Care Program.

The Director is ex-officio chairman, and eight other members (five of whom must be specialists in the field of medical and hospital care, and four doctors of medicine are to be appointed by the Administrator.

The Director is authorized to utilize the services and facilities of any executive department or agency.

### V. Dental Health Services (Title VIII)

This portion covers dental health services for school children and provides for increasing appropriations as grants-in-aid from the Federal government: \$1,000,000 for surveys and annual amounts ranging from \$8,000,000 for the first year to \$20,000,000 at the end of five years. The requirements for grants-in-aid for dental programs are similar to those for medical and hospital care and for school inspection.

(Continued on Page 605)



*Borden's prescription specialties are flexibly adaptable to cope effectively with the sharply increased number of your infant feeding problems.*

**BIOLAC**—a complete infant formula (only vitamin C supplementation needed) for infants deprived of mother's milk.

**DRYCO**—a powdered, high-protein, low-fat, moderate carbohydrate milk food ideally suited for all formulas.

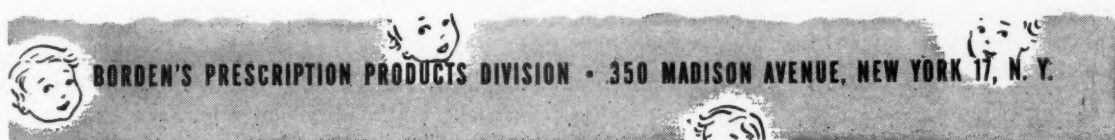
**BETA-LACTOSE**—an exceptionally palatable, highly soluble milk sugar for formula modification.

**MULL-SOY**—a hypo-allergenic emulsified soy food for infants and adults allergic to milk proteins. The 1:1 standard dilution approximates cow's milk in fat, protein, carbohydrate and mineral content.

**KLIM**—a spray-dried whole milk with soft curd properties essential in infant feeding and special diets. Particularly valuable when availability or safety of fresh milk is uncertain.



*Borden prescription products are available at all drug stores. Complete professional information may be obtained on request.*





# Michigan Postgraduate Clinical Institute

The registration at the 1947 Institute in Detroit totalled 1,293. The breakdown follows:

Doctors of Medicine.....	1,082
Guests and Exhibitors.....	211

TOTAL .....	1,293
-------------	-------

A total of 113 out-of-Michigan Doctors of Medicine came from nine states, as follows: 47 from Ontario, 40 from Ohio, 12 from Indiana, 8 from Wisconsin, 2 from Illinois, and 1 each from California, Iowa, Louisiana and New York.

A total of 9,317 lines of publicity appeared in Detroit and Michigan newspapers in connection with the Michigan Postgraduate Clinical Institute of 1947!

## UNSOLICITED COMMENTS RE THE MICHIGAN POSTGRADUATE CLINICAL INSTITUTE

*R. A. Fargher, M.D.*, of LaPorte, Indiana: "I am writing to tell you how much we enjoyed and how much benefit we received from our visit to Detroit this past week. The two of us from here who attended felt that we were greatly repaid in information for the effort we put forth in coming. It is my contention that we men in general practice do not have enough such opportunities to keep up on things; I hope there will be a Michigan Postgraduate Clinical Institute to attend next year."

*D. H. Bruns, M.D.*, of Milwaukee, Wisconsin: "I am grateful for having been privileged to participate in the first annual Michigan Postgraduate Clinical Institute. Both the scientific and practical presentation of chapters of nearly every field of medicine was inspiring. If permitted, I certainly will attend your next year's Institute."

*John M. Dorsey, M.D.*, Detroit: "The responsibility of being of service in our great Michigan Postgraduate Clinical Institute was very much of the nature of a fine privilege. May I take this occasion to thank you and to advise that the opportunity to be able to be a little helpful pleased me. I wish you continued success with the Michigan Postgraduate Clinical Institute."

*F. E. Carrel, M.D.*, of Frankfort, Indiana: "Believe me, it was refreshing to hear those twenty-minute lectures without listening to history and statistics. The many things learned have already had numerous application with the result of more satisfied patients."

*B. B. Backley, M.D.*, of Lakewood, Ohio: "I enjoyed the Michigan Postgraduate Clinical Institute very

much and am looking forward to the 1948 Institute. I wish to express my thanks for your inviting to the first, recent Institute. I shall try to promote more interest among the fraternity here to attend the second session next March.

*Raymond T. Saxon, M.D.*, Hicksville, Ohio: "The 1947 Michigan Postgraduate Clinical Institute was very highly practical and instructive to a general practitioner like myself. It is indeed a pleasure to attend a session in which there is a departure from the papers on rare and infrequent conditions. I am very hopeful that meetings of this caliber will be permanent annual affairs."

*James L. Henderson, M.D.*, Detroit: "I consider the Michigan Postgraduate Clinical Institute the most concise and generally beneficial postgraduate study offered to Michigan doctors in my 33 years of practice."

*R. A. Wagner* of Smith, Kline & French Laboratories, Philadelphia: "Our representatives who attended the first annual Michigan Postgraduate Clinical Institute told me of the success of it—of the physicians' interest in the technical exhibits and of the splendid co-operation of the convention management. We shall indeed look forward to attending again next year."

*J. A. Lutz* of W. B. Saunders Company, Philadelphia: "Congratulations on the success of the first annual Michigan Postgraduate Clinical Institute. Of course we want to attend the 1948 Institute and all future Institutes, so send us an invitation every year."

*R. O. Johnson* of Farnsworth Laboratories, Chicago: "We are very happy for having attended the Michigan Postgraduate Clinical Institute. You made a fine job of it. Thank you for your splendid co-operation. I am looking forward to the 1948 Institute and we want to be entered now as a participant."

*R. V. Oosting* of Medical Arts Surgical Supply Company, Grand Rapids: "I want to take this opportunity to congratulate you on the very fine Michigan Postgraduate Clinical Institute so ably conducted in Detroit. I would like to make reservation for our attendance next year."

*J. W. Colen* of J. B. Lippincott Company, Philadelphia: "It is with a great deal of pleasure, that I write you advising we consider the Michigan Postgraduate Clinical Institute, recently held in Detroit, as a very successful meeting."

*Morton Hack* of Hack Shoe Company, Detroit: "The Michigan Postgraduate Clinical Institute provides an excellent opportunity for reiterating our so-often ex-

(Continued on Page 512)





"A person's nutritional status today depends on the events of all past days."<sup>1</sup> Slight deficiencies should not be ignored "as if they were without effect," for "partially, indeed slightly deficient diets eaten regularly and periodically over many years have their consequences."<sup>1</sup> Such nutritional delinquency often takes its greatest toll under the stress of illness, surgery, pregnancy, lactation, or accident. For depleted tissues, Upjohn vitamins provide a wide range of dosage forms for therapy or supplementation, in preparations adapted to oral and parenteral administration in the practice of medicine and surgery.

<sup>1</sup> National Research Council  
Bull. No. 109, 1943, pp. 18-21.



FINE PHARMACEUTICALS SINCE 1886

U P J O H N V I T A M I N S

MAY, 1947

Say you saw it in the *Journal of the Michigan State Medical Society*

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# MICHIGAN POSTGRADUATE CLINICAL INSTITUTE

(Continued from Page 510)

pressed appreciation for your many courtesies over the years of our association. The Hack Clan rated the recent Institute as 'tops.' "

## RECORD OF ATTENDANCE

Postgraduate credits: one unit of credit for each day of postgraduate attendance was given every member of the Michigan State Medical Society registering at the first annual Michigan Postgraduate Clinical Institute. The following MSMS members registered on March 12 (the registrations of March 13 and March 14 will appear in a subsequent Number of JMSMS).

### Registration—March 12

Vernon C. Abbott, Pontiac; James R. Adams, Dearborn; E. R. Addison, Crystal Falls; Sidney L. Adelson, Detroit; Alfred L. Aldrich, Ithaca; Allen Alexander, Detroit; Herbert C. Allison, Gross Pointe; Sam Alpiner, Detroit; Abraham Altschuler, Detroit; Emil Amberg, Detroit; Florence Ames, Monroe; Walter L. Anderson, Detroit; F. T. Andrews, Bay City; Howard B. Appelman, Detroit; Robt. J. Armstrong, Kalamazoo; Harry Arnkoff, Pontiac; Emilie Arnold-Clarke, Lansing; R. J. Arrington, Detroit; S. R. Ashe, Detroit; A. U. Axelson, Detroit.

Walter F. Bach, Detroit; M. E. Bachman, Detroit; Vinton A. Bacon, Detroit; Harry E. Bagley, Dearborn; William A. Bailey, Detroit; William J. Bailey, Detroit; Clarence Baker, Detroit; George M. Baker, Parma; Robert H. Baker, Pontiac; Joseph A. Bakst, Detroit; Harry Balberur, Detroit; Charles W. Balser, Detroit; Lewis R. Barak, Detroit; Harry A. Barbour, Mayville; R. H. Baribeau, Battle Creek; Oscar L. Barland, Detroit; S. E. Barnett, Detroit; Chas. J. Barone, Detroit; Winona Barrows, Royal Oak; William A. Barss, Detroit; F. W. Bartholic, Homer; F. W. Baske, Flint; Paul H. Bassow, Ann Arbor; Ernest W. Bauer, Hazel Park; L. E. Bauer, Detroit; Colin Beaton, Detroit; W. G. Beattie, Ferndale; Abraham Becke, Detroit; L. E. Beeuwkes, Dearborn; Warren F. Belknap, Royal Oak; Wm. M. Bell, Detroit; George W. Bennett, Elsie; S. A. Bennett, Detroit; Z. B. Bennett, Detroit; John C. Benson, Flint; John C. Benson, Jr., Flint; Virginia M. Benson, Detroit; Frederick Bentley, Plymouth; Richard H. Berg, Oxford; H. L. Bergo, Detroit; Robert Berman, Detroit; Albert E. Bernstein, Detroit; E. A. Bicknell, Detroit; G. C. Bishop, Almont; Kenneth E. Blain, Detroit; E. W. Blanchard, Decker-ville; D. C. Bloemendaal, Zeeland; P. W. Bloxsom, Grand Rapids; Arthur F. Boell, Detroit; A. T. Bonathan, Flint; A. M. Bookstein, Detroit; Carl F. Boothby, Hartford; P. R. Boothby, Lawrence; T. A. Boutrous, Detroit; Fred C. Brace, Grand Rapids; Andrew H. Bracken, Dearborn; H. A. Brady, River Rouge; F. W. Bramigk, Detroit; Walter A. Briegel, Detroit; William Bromme, Detroit; C. W. Brooks, Detroit; John Bryce, Detroit; W. Paul Buchanan, Detroit; John D. Buck, Detroit; F. G. Buesser, Detroit; F. L. Bull, Sparta; Bert M. Bullington, Saginaw; J. G. Burdick, Allegan; W. M. Burling, Grand Rapids; Julius N. Burnstine, Detroit; Harry J. Butler, Detroit; G. M. Byington, Detroit.

J. Ewart Caldwell, Detroit; Ethel T. Calhoun, Pontiac; Duncan Campbell, Detroit; P. F. Carlucci, Detroit; Joseph Carp, Detroit; E. I. Carr, Lansing; Fred E. Caurmartin, Detroit; Henry G. Chall, Detroit; M. S. Chambers, Flint; W. A. Chipman, Detroit; Joseph W. Christie, Pontiac; Ronald E. Clark, Detroit; Norman E. Clarke, Detroit; Robert W. Claytor, Grand Rapids; John H. Cobane, Detroit; Edgar G. Cochrane, Detroit; H. Herbert Cohen, Detroit; W. C. C. Cole, Detroit; Raymond W. Conn, Detroit; Frank O. B. Connolly, Detroit; C. G. Constable, Detroit; R. C. Conybeare, Benton Harbor;

William L. Cooper, Fort Custer; Goldie B. Corneliuson, Lansing; Louis D. Cotruro, Detroit; F. Cox, Jackson; Ronald E. Crissey, Detroit; G. D. Cummings, Lansing; James E. Curlett, Roseville; J. H. Curtin, Flint; Arthur C. Curtis, Ann Arbor; Russell G. Cushing, Detroit.

W. A. Dawson, Inkster; John C. DeMeulenaere, Detroit; Joe. De Pree, Grand Rapids; Paul E. Derleth, Detroit; R. E. deSpelder, Detroit; Paul L. DeWacle, Bay City; Harry F. Dibble, Detroit; B. R. Dickson, Detroit; Bernard Dickstein, Flint; Panfilo C. Diloreto, Detroit; Frank Diskin, Muskegon; E. F. Dittmer, Detroit; R. C. Dixon, Pigeon; Ray S. Dixon, Detroit; F. E. Dodds, Flint; C. F. Dodenhoff, Detroit; S. W. Donaldson, Ann Arbor; Leo C. Donnelly, Detroit; Clarke Dorland, Lapeer; V. Droock, Detroit; Gordon A. Dumas, Detroit; E. M. Dundas, Detroit; Robert H. Durham, Detroit.

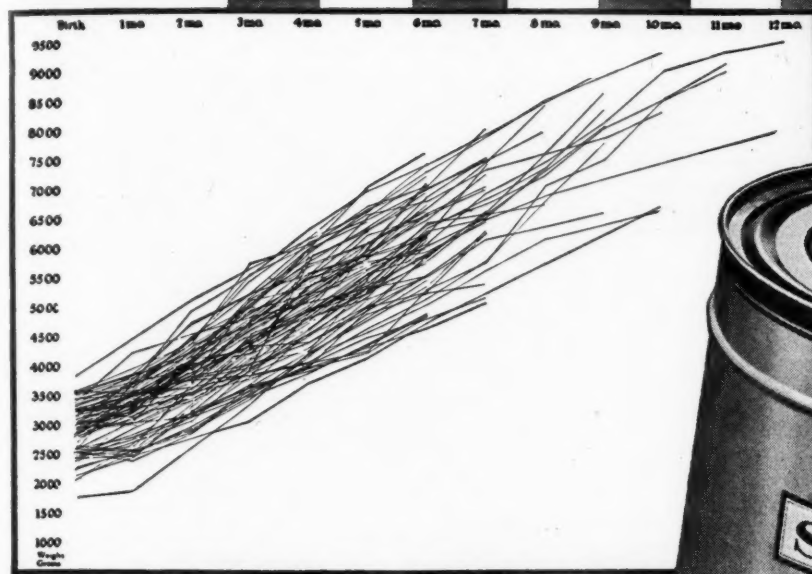
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# The JOURNAL

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## Serodiagnosis of Syphilis

### Recent Advances

By Charles R. Rein, M.D.  
New York, New York



PRACTICING PHYSICIANS have had the problem of how to evaluate or interpret serologic reports obtained from the laboratory in determining the presence or absence of a syphilitic infection. Every physician has probably had patients with clinical syphilis in whom the serologic tests gave negative reactions, as well as nonsyphilitic patients with unexplained positive serologic reactions. Such discrepancies are to be expected, since it is well known that there are no true specific tests for syphilis. When Wassermann, Neisser and Bruck<sup>42</sup> developed the first serologic test for syphilis some forty years ago, they felt that they had devised a specific and a sensitive laboratory procedure for the diagnosis of syphilis. They considered their test specific because they employed a saline extract of *syphilitic* liver for the antigen. They thought it was adequately sensitive because positive reactions were obtained with the blood of many individuals with active clinical syphilis. It was, however, soon discovered that not only were these antigens nonspecific, but that alcoholic lipid extracts obtained from normal tissue were more specific and more sensitive than the aqueous ex-

tracts of syphilitic tissues. Fortunately the combined efforts of research-minded serologists and clinicians have done much to improve those procedures which are employed today in the serodiagnosis of syphilis.

Considerable progress has been made in the laboratory, in the proper interpretation and the clinical application of these serologic procedures. I will briefly describe the improvement made in laboratory techniques and in materials employed.

**Collecting Tubes.**—The use of wet and non-sterile syringes in the collection of blood specimens rendered many of them unsatisfactory for serologic testing. The development of inexpensive dry and clean vacuum tubes for the collection and mailing of blood specimens has done a great deal to decrease the number of unsatisfactory specimens received by the laboratory. Sterility is not an absolute necessity when clotted bloods are shipped, since the clot seems to exert a bacteriostatic effect on the serum. It is important, however, that the collecting and mailing tubes be clean and dry.

**Serum Preservatives.**—In warm climates, clotted blood specimens become hemolyzed and may therefore become unsatisfactory for testing. Army facilities found it necessary to separate the serums from the clots to eliminate hemolysis. Frequently it was necessary to ship these serum specimens to distant laboratories, and it was sometimes quite difficult and often impossible to insure sterility in the collection and preparation of serum. During the several days it took for the specimens to reach the laboratory they became badly contaminated and unsatisfactory for testing. It was deemed necessary to find a suitable substance which would prevent this contamination and not interfere with serologic testing. Merthiolate answered this need. Merthiolate (sodium ethyl mer-

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curi thiosalicylate) is an excellent bacteriostatic and bactericidal agent for the preservation of serums, and for the past several years has been employed by the United States Public Health Service and other agencies for the preservation of serum and spinal fluid specimens intended for shipment over considerable distances. In the Division of Serology at the Army Medical School,<sup>34</sup> sera preserved with one mg. of merthiolate per millimeter have been used routinely with excellent results. The use of merthiolate as a preservative in army laboratories has markedly decreased the number of specimens rendered unsatisfactory for serologic testing because of bacterial contamination. During the past three years more than 20,000 merthiolated specimens have been received at the Division of Serology for special serologic studies, and less than 0.1 per cent were unsatisfactory for testing because of bacterial contamination.

*Inactivation of Serum.*—For many years it was believed that it was not necessary to heat or "inactivate" serums prior to testing with the various flocculation tests, and that such "inactivation" was only necessary to destroy the native complement present in fresh serums when tested with the complement-fixation procedures. Recent studies at the Army Medical School<sup>37</sup> have indicated that fresh syphilitic serums contain a thermolabile substance which inhibits or retards the aggregation of lipoidal antigens in flocculation reactions. Strongly positive serums would often give negative reactions when tested in the raw or unheated state. It was found that all serums had to be heated<sup>36</sup> before testing with complement-fixation or flocculation procedures. Serums heated for ten minutes at 56° C., for one minute at 69.5° C., and seven seconds at 100° C. (in boiling water) gave results that were practically identical with those obtained with serums heated for the routine thirty minutes at 56° C. The unnecessary prolongation of the heating period tends to destroy some of the reagin in the serum. The rapid preparation of serum in this manner is especially valuable as a time-saving factor where the rapid flocculation tests are used for the detection of syphilis in donors just prior to transfusion.

*Antigens.*—Considerable progress has been made in the improvement of the various lipoidal an-

tigens. The isolation by Pangborn<sup>26,27,29</sup> of the substance cardiolipin from beef heart and the development of methods for the purification of lecithin<sup>28</sup> prepared from both heart and egg yolk promised to contribute much to the improvement of serodiagnostic tests for syphilis. Several investigators, Harris and Portnoy,<sup>8</sup> Harris, Rosenberg and Reidel,<sup>9</sup> Kline,<sup>10</sup> Brown,<sup>2</sup> the Maltaners<sup>22</sup> have described the preparation of cardiolipin antigens for use in the various complement-fixation, macro and microflocculation tests. At the Army Medical School, a cardiolipin antigen<sup>33</sup> was successfully adapted for use in a microflocculation slide test for the serodiagnosis of syphilis. The sensitivity of this test was higher than that obtained with the Kline diagnostic, Mazzini, Kahn and Kolmer tests. It was of interest to note that this increased sensitivity was obtained without any apparent increase in nonspecificity. In fact, the extraordinary specificity of the cardiolipin antigen in the presence of malarial infection was repeatedly demonstrated.

*Preserved Sheep Blood.*—One of the difficulties encountered in the performance of complement-fixation tests is in obtaining satisfactory sheep blood. The smaller hospital laboratories with no facilities for the raising of sheep have to obtain their supply from the slaughter house. Many times the red blood cell suspensions prepared from such sheep blood prove to be unsatisfactory. A preservation technique for maintaining uniformity in the properties of sheep cells would be a great laboratory convenience. It would be advantageous to employ preserving fluids which would maintain the properties of sheep blood over long periods and particularly during periods of transportation. Quantitative studies at the Army Medical School indicate that aseptic collection of sheep blood in modified Alsevers' solution<sup>3</sup> at ordinary temperatures and subsequent refrigeration permit the preservation of the blood for several months without the development of appreciable hemolysis or change in susceptibility to lysis by guinea pig complement and rabbit amboceptor. Blood collected in this fashion has been used for the past two years with complete satisfaction.

*Spectrophotometer.*—Accurate standardization of the hemolytic system in the complement-fixation tests has become of paramount importance in maintaining a constant level of sensitivity. To



this end the spectrophotometer has been adapted,<sup>18</sup> not only for quantitative titration of complement and amboceptor, and for the standardization of sheep cell suspensions, but also for the final readings of the tests themselves. The use of this instrument has been adapted for the complement-fixation test for syphilis as well as for complement-fixation tests employed in the serodiagnosis of other diseases, such as malaria and amebiasis.

**Amboceptor.**—The preparation of antsheep amboceptor with the elimination of rabbit shock has also proved advantageous to laboratories performing complement-fixation tests. The chief difficulty in preparing amboceptor has been the heavy loss of rabbits by shock, particularly following the injection of the second dose of cells. Furthermore, when whole cells are employed, the finished amboceptor may contain relatively large amounts of agglutinogens or precipitins, rendering it unsatisfactory for use. A method<sup>38</sup> was developed at the Army Medical School for the preparation of antsheep amboceptor utilizing the cell stroma instead of the packed washed cells. The stroma is prepared by specifically hemolyzing washed sheep cells with amboceptor and complement. During five years of use with over 500 animals, there have been no rabbit deaths due to shock. Satisfactory amboceptor has been produced in about ten days, and the titers are higher than those obtained by other methods.

**Complement.**—The majority of small laboratories do not have facilities for maintaining their own colony of guinea pigs which are necessary for their supply of guinea pig complement. Dried or lyophilized guinea pig serum has been used at the Army Medical School in various types of complement-fixation tests with excellent results. Dried guinea pig complement supplied to the Army Medical School had to meet the following requirements:

1. **Titer:** The exact hemolytic unit should be contained in no more than 0.45 ml. of a 1:30 dilution when titrated by the Kolmer method.
2. **Moisture content:** Should not exceed 1 per cent by weight.
3. **Hemoglobin content:** Should be minimal.
4. **Source of guinea pigs:** The serum should be obtained from normal healthy guinea pigs

which have never been used for any other purpose.

5. **Preserving fluid:** Supplied with the dried product should contain 6 per cent sodium acetate and 2 per cent boric acid.

Several commercial concerns prepare dried guinea pig complement which meet the above requirements and give satisfactory results.

**Serum Controls.**—A positive and negative serum control should be included every time serologic examinations are made. This helps to insure the sensitivity and specificity of the test employed and tends to minimize the occurrence of technical errors. Unfortunately, many laboratories select a strongly positive serum for their control. Such controls are unsatisfactory for detecting a decrease or increase in the sensitivity of a serologic procedure, for if the sensitivity has been reduced or increased as much as 50 per cent, a strongly positive serum might still give a four-plus reaction. The use of weakly positive or partially positive serums would more readily detect a change in sensitivity due to technical errors or to deterioration of materials employed. If strongly positive serums are utilized, they should be subjected to serial dilutions and the test performed on each dilution. A reduction or increase in *titer* would indicate a change in sensitivity. The utilization of a strongly positive serum (quantitative control) or weakly positive serums (qualitative controls) is of utmost importance in controlling the sensitivity level of a serologic procedure.

There have been many more improvements such as the use of recalcified plasma instead of serums for serologic testing, the use of the 50 per cent hemolytic unit instead of 100 per cent end point of hemolysis in determining the degree of fixation of complement by specific antigen-antibody complex, the introduction of the new wetting agents for the proper washing of serologic glassware, the use of buffered solutions in preparing the antigen emulsions, complement and amboceptor dilutions and for diluting strongly positive serums for the various quantitative tests, the prevention of non-specific and prezone reactions in the complement-fixation test with spinal fluid by the addition of egg albumen or normal serum to the complement, and the development of special procedures to differentiate between true and false positive reactions. Suffice to say that all of these advances have

helped considerably in the improvement of our serodiagnostic procedures.

### Serologic Surveys

Together with the technical advances made, definite progress has also been made in the interpretation and clinical application of serodiagnostic procedures. Many modified methods of complement fixation and flocculation tests have been described and accepted during the past forty years. It must be understood that although these tests are identified by individual names they are not *unrelated* reactions. All depend on the same mechanism of combination of the syphilitic reagin with the lipoid antigen. Each serologist has attempted, however, by various means to make his test more sensitive, more specific, more constant or simpler in technical performance. Many have succeeded in one or more of these improvements. Others, however, have improved one factor at the expense of others, and as a rule their tests are soon discarded. Unfortunately, a new test sometimes falls into the hands of serologists and even practicing physicians before its efficiency has been proved, and considerable harm is done to unsuspecting patients before the tests are standardized or abolished. The basis for selection of suitable standard tests to be used in the serum diagnosis of syphilis has been the accumulated data, regarding the efficiency of the many tests evaluated in the various official serologic conferences. The United States Public Health Service, in collaboration with the American Society of Clinical Pathologists, has had a number of evaluation studies to appraise the various tests employed in this country. These studies have done a great deal to determine the unsatisfactory tests and to encourage the participating serologists to improve the specificity and sensitivity of their respective procedures. Criteria have been established for adequate specificity and sensitivity, and only tests conforming to these standards should be used for the routine serodiagnosis of syphilis. With increased sensitivity it has been possible to detect more syphilitic individuals *very early* and *much later* in the course of their infection.

### Penicillin Therapy in Concomitantly Acquired Gonorrhea and Syphilis

With the introduction of penicillin, the physician now has at his disposal a therapeutic agent which is efficacious in the treatment of gonorrhea

and syphilis. When penicillin was adopted by the Armed Forces as the standard treatment for gonorrheal infections, it was anticipated that a concomitantly acquired syphilitic infection would be masked by the penicillin, and many reports of this type have appeared in the literature. In most instances the patient acquired syphilis concomitantly with the gonorrheal infection. Promiscuous patients, however, may acquire syphilis immediately prior to or soon after becoming infected with gonorrhea. The amount of penicillin (usually 200,000 to 400,000 units) which is adequate for the cure of gonorrhea is definitely inadequate for the concomitant syphilitic infection. In such patients the following may occur:

*Abort.*—If the patient received penicillin very early in the course of the gonorrheal infection, and the syphilis is only of a few days' duration, that relatively small amount of penicillin may be sufficient to abort or cure the syphilitic infection. This has been corroborated by animal experiments where small amounts of penicillin administered a few days after infection were sufficient to effect a cure.

*Mask.*—If the concomitant syphilitic infection is a few days older, the same amount of penicillin may prevent the appearance of the primary or secondary lesions. In such instances the only evidence of a syphilitic infection is the development of positive serologic tests for syphilis several weeks or months following treatment of the gonorrheal infection.

*Delay.*—In still older infections the penicillin therapy will tend to delay the appearance of the early cutaneous manifestations for several months after the disease has been acquired.

Some investigators<sup>7,21</sup> have observed the occurrence of chills, fever and malaise developing early in the course of penicillin therapy for gonorrheal patients who also have a syphilitic infection. They believe these symptoms indicate a Herxheimer reaction due to the rapid destruction of the spirochetes, the incidence and severity of the reactions depending upon the extent of the spirochetal invasion. It has been suggested that the following be done whenever penicillin therapy is instituted for gonorrheal infections: (1) thorough examination for any clinical evidence of syphilis and the performance of a serologic test

prior to the administration of therapy, (2) observations for the occurrence of chills, fever and malaise accompanying penicillin therapy, and (3) repeated clinical and serologic re-checks at monthly intervals for six months following therapy. If, at any time during this period there is any clinical or serologic evidence of syphilis, additional adequate penicillin therapy should be administered.

### Serologic Response in Penicillin-Treated Syphilis

Physicians are often disappointed when serologic tests remain positive for several months following penicillin therapy for syphilis. There are, however, several factors which influence the length of time required to attain sero-negativity.

*Stage of Disease.*—The older the disease, the longer spirachetes are present and the longer it takes for the body cells to stop forming reagin. As a rule patients with secondary syphilis require more time to acquire sero-negativity than patients with sero-positive primary lesions.

*Immunologic Response of Individual Patients.*—Some patients with syphilis develop more antibodies or reagin than do others after the same type of stimulus. The former patients usually require more time to attain sero-negativity.

*Serologic Titer.*—As a rule, patients with high serologic titers at the onset of therapy may require more time than those with relatively low titers to attain sero-negativity.

*Sensitivity of the Serologic Procedure.*—The more sensitive the serologic test, the longer it will take to attain sero-negativity. When a serologic battery consisting of tests with varying sensitivities is employed, negative reactions may be obtained with the less sensitive tests long before the more sensitive tests become negative.

*Type of Test.*—Certain types of tests may remain positive long after other tests have become negative, even though they may be of the same relative range of sensitivity.

*Treatment Schedule.*—The amount of therapy and the length of time required to administer that amount of treatment may also affect the length of time to attain sero-negativity. As a rule, the higher the total dosage of penicillin and the longer the period of time during which the treatment is

administered, the shorter the time to attain sero-negativity.

It must be pointed out, however, that there are many variations to the above factors, and no set rules can be made to determine or anticipate the length of time required to attain sero-negativity. Thomas<sup>39</sup> believes that patients who continue to have persistent strongly positive serologic reactions nine months after rapid therapy, should be re-treated as a precautionary measure. He emphasized the fact that one should not expect rapid reductions in serologic titers in such patients after re-treatment.

### Serologic Differentiation Between Relapse and Re-infection

With the introduction of various forms of rapid treatment for early syphilis, many more patients are attaining serologic and clinical cures earlier than heretofore. Such patients are candidates for re-infections, and it is not an infrequent occurrence to find patients re-infected with their own spirochetes. This type of re-infection is very aptly called "ping-pong" syphilis. The individual acquires syphilis extramaritally and, after the development of the primary lesion, infects his marital partner. He receives adequate penicillin therapy and may attain a clinical and serologic cure within several weeks. During this time his wife has been incubating the spirochetes and re-infects him with his own spirochetes on subsequent sexual exposure.

The criteria for re-infection are quite rigid and, unfortunately, the patients are not observed at sufficiently frequent intervals to satisfy all of these requirements. It is, therefore, often quite difficult to determine whether such patients have developed a new infection or if there has been a relapse of the old infection.

At the Army Medical School we have had considerable experience with the serologic follow-up of patients with penicillin-treated early syphilis. A battery of serologic tests were performed with serums of such patients at weekly and monthly intervals. From our observations we feel it is possible to distinguish between relapse and re-infection by carefully conducted serologic studies at frequent intervals. Following penicillin therapy in patients with early syphilis, there is usually a progressive reduction in serologic titer. In re-infection the patient usually attained and maintained complete sero-negativity followed by the development of a dark field positive, sero-negative



lesion at a new site. Shortly afterwards such patients developed sero-positive reactions with rapidly increasing titers. In treatment failures or relapse there was noted a sudden increase in serologic titer followed in about one month by clinical evidence of a muco-cutaneous relapse. If penicillin-treated patients would be subjected to serologic examinations at weekly or monthly intervals, it might be possible to predict a clinical relapse about one month before there is any clinical evidence, by a progressive increase in serologic titer on repeated examinations.

It is of utmost importance, therefore, to educate patients of the great need of reporting to physicians for serologic and clinical examinations at regular monthly intervals for at least one year following the completion of penicillin therapy.

#### Serologic Differentiation Between Prenatal Syphilis and Syphilotoxemia

Due to legislation passed by many states requiring routine prenatal blood testing, there has been an increased interest in the status of the offspring born of the syphilitic mother. These children may show no evidence of syphilis other than a positive serologic test. Many infants from adequately treated syphilitic mothers are subsequently proven to be nonsyphilitic even though positive serologic reactions are obtained with the cord or venous blood at birth. It is in this group that most errors in diagnosis have been made. Such infants do not have a true syphilitic infection, but the presence of reagin in the infants' blood is evidence of a transient syphilotoxemia. This type of reagin usually disappears within the first month of life, but may persist as long as three months.<sup>5,15</sup>

Serologic tests for syphilis in sero-positive infants should be performed at frequent intervals for a period of three months. If the tests become less positive or negative without specific treatment during that period, it is reasonable to consider that the infant is nonsyphilitic. If, however, the blood tests are positive at birth and remain positive, or if they are originally sero-negative and become positive by the end of the third month, it may be considered as indubitable evidence that the infant is syphilitic regardless of the serologic status of the mother. A comparison of the serologic titers of the mother and infant may be of great aid in determining the final status of the child. In the absence of any other evidence of prenatal

syphilis (positive dark field examination of the umbilical cord, roentgenographic evidence of syphilitic bone involvement, or cutaneous manifestations of syphilis) antisyphilitic therapy should be withheld for at least three months.

It is unnecessary to collect the blood by venipuncture for each serologic examination, since sufficient blood can be obtained from a deep puncture wound of the infant's heel for the performance of a microflocculation test requiring only 0.05 ml. of serum.

#### Value of Routine Serologic Examinations

Most states now have laws requiring a serologic examination prior to marriage. These premarital laws have been quite worth while in detecting unsuspected cases of syphilis, but they have their limitations. For example, some states still forbid marriage of sero-positive individuals regardless of whether or not they are infectious. This is a serious mistake, since the majority of these individuals are in the latent and noncommunicable stage of the disease. The decision as to whether an individual is in the infectious stage should rest with the physician, and he must decide if and when that individual may enter into marriage.

The importance of educating pregnant women to have a blood test as early as possible in their pregnancy cannot be overemphasized. The early detection of a syphilitic infection and the early and adequate administration of antisyphilitic therapy can and will prevent prenatal syphilis. Unfortunately, most laws do not require serologic examinations on newborn infants, and thus the advantage of the early detection and treatment of prenatal syphilis is lost.

There has been an increasing trend to routine serologic examinations of employees prior to employment and of applicants prior to the issuing of insurance policies. This is of value in detecting unsuspected cases and in directing them for treatment. It is important, however, to discourage the employer from refusing employment or for insurance companies from refusing to issue life insurance policies because the individual has a positive blood test.

Undoubtedly, serologic examination on induction into and separation from the armed forces uncovered a large number of persons with unsuspected syphilis. Adequate treatment will certainly prevent the occurrence of the serious late

sequelae of syphilis in the majority of these individuals.

### Limitations of Serodiagnostic Procedures for Syphilis

While it is true that most positive serologic reactions obtained with our current nonspecific lipid antigens are due to syphilis and perhaps represent some type of immunologic response, it is no less true that some positive results are unrelated to syphilis and represent a general biologic phenomenon. Such *false positive* or nonspecific reactions may be caused by a variety of infectious diseases, immunizations and metabolic disturbances. It has also been shown that similar nonspecific (nonsyphilitic) reactions may occur in individuals who show no evidence of any pathologic state. Since false positive reactions may occur in the absence of syphilis, unquestionably many persons have been stigmatized and have been given treatment solely on the basis of positive reactions disclosed by routine serologic examinations, in the course of, or immediately following, a nonsyphilitic disease. Compulsory preinduction, prenatal, premarital serologic examinations, and the increasing widespread use of routine blood testing in medical practice, industry, and on separation from the armed forces, have undoubtedly increased the number of individuals needlessly subjected to antisyphilitic treatment.

Since serodiagnostic tests are not truly specific for syphilis, the physician must be aware of which conditions, other than syphilis, may produce nonspecific (nonsyphilitic) reactions. Such reactions may be either technical or biologic. Technical false positives may occur in serums containing no antibodies and may be due to (1) technical errors in the collection and labeling of specimens, (2) the use of unsatisfactory blood specimens (contaminated or hemolyzed), (3) errors in the performance of the serologic tests, (4) the use of faulty materials and reagents in the test or (5) errors in recording or reporting the final results. With the improvement of serologic techniques and the use of improved materials, especially purified antigens of the cardiolipin type, there has been marked reduction in the incidence of technical false positives.

Biologic false positives are due to (1) the presence of antibody-like substances similar to the antibodies produced in syphilitic diseases, (2) an increase or alteration of the sero-globulin frac-

tion or (3) an increase or alteration of some chemical substance or substances in the blood.

As a result of a series of studies at the Army Medical School, it was found that there are a number of factors involved in the incidence of false positive reactions for syphilis.<sup>35</sup> Time does not permit a discussion of all of these factors, but it was found that almost any condition may evoke a nonspecific reaction in a susceptible individual (serologic reactor). A number of procedures have been suggested to establish the existence of nonspecific reactions. Since the majority of these reactions are of the transient type and revert to sero-negativity within a short period of time, it is suggested that all individuals with positive serologic reactions for syphilis, unconfirmed by history or clinical evidence, should be followed serologically and without treatment for a period of three months, serologic tests being performed at two- to four-week intervals. At the end of that time the patient should be completely re-appraised to ascertain whether or not syphilis may be present. A continuing drop in serologic titer in a relatively short period of time, without the administration of antisyphilitic treatment, is strong evidence in favor of nonspecific serologic reactions. Irreparable harm has been done by an ill-considered or hasty diagnosis. If treatment is started prematurely, the evidence which could finally lead to an accurate diagnosis is often obscured. Serologic tests may become negative with a few injections, and one is at a loss to know whether the sero-negativity represents response to therapy or merely reflects the fact that the patient never had syphilis.

Another serious limitation of our serodiagnostic procedures is the occurrence of *false negative* reactions. When the serum of a patient with clinical syphilis gives a negative reaction, that patient is said to have sero-negative syphilis, and the reaction is considered as falsely negative. Actually the serum contains so little reagin that the particular test used is unable to detect its presence. Yet, if that same serum is re-checked by a more sensitive test, it would frequently yield a positive reaction. Such discrepancies are often observed in patients with primary syphilis. After the development of the primary lesion, the serum may give negative reactions with the insensitive tests for three weeks or longer, while with the more sensitive tests, a positive reaction may be obtained

within a few days after the appearance of the chancre. In an unpublished study<sup>32</sup> of experimental syphilis in rabbits, it was possible to detect the evidence of syphilis by means of a sensitive serologic test as much as five days before the clinical appearance of the chancre. This suggests, at least, that reagin begins to appear in the blood serum soon after inoculation with the *treponema pallidum*, but the routine tests are not sufficiently sensitive to detect their presence. Therefore, the incidence of sero-negative primary syphilis does not depend only on the time which has elapsed since inoculation, but more so on the sensitivity of the tests employed.

The same holds true in sero-negative late syphilis. It is not uncommon to find that patients with syphilis of the aorta may have negative blood tests. In the literature there are reports that the incidence of sero-negative cardiovascular syphilis and neurosyphilis is as high as 40 per cent. This high incidence is based on the fact that the tests used in these investigations were relatively insensitive. When the very sensitive tests are used, the incidence of negative reactions is markedly decreased. Therefore the number of cases of sero-negative late syphilis does not depend on the clinical manifestations of syphilis, but rather on the sensitivity of the particular tests. Yet even with the most sensitive tests available today, one occasionally obtains a negative reaction in a patient with clinical syphilis. The clinician, therefore, must be careful in the interpretation of serologic reports because syphilitic patients may give negative reactions.

Sero-negative syphilis may be due to a number of factors, as (1) the amount of antibody is minimal and cannot be detected by tests with ordinary sensitivity, (2) the presence of too much antibody so that false negative zone reactions occur, (3) the use of serologic tests with low levels of sensitivity, (4) the use of fresh serum containing considerable amounts of thermolabile-inhibiting substances, and (5) the presence of a thermostabile-inhibiting substance in the albumin fraction of the serum.

### Verification Tests in the Serodiagnosis of Syphilis

The difficulties of basing a diagnosis of syphilis on current serodiagnostic tests alone have been pointed out by Moore, Eagle, and Mohr.<sup>23</sup> They have suggested some sixteen procedures of value in differentiating true from false positive reactions. Many of these procedures require special

clinical and laboratory techniques, and often necessitate weeks or months of observation and expert syphilologic advice. In view of these conditions there is need for a method which will differentiate the false from the true reactions. Several "verification" or "confirmation" procedures have been proposed for this purpose.<sup>10-12,16,17,40,41,43</sup> Investigators<sup>4,6,24,31</sup> have reported that antigens for complement-fixation tests made from cultured spirochetes are far more specific than tissue extract antigens. Other investigators<sup>13,14,20</sup> have found the spirochetal test to be no more specific than the routine tests. In the Washington Serology Conference<sup>30</sup> both Richter and Eagle participated with spirochetal antigen complement-fixation tests as well as with the standard procedures employing lipoid antigens. More false positive serologic reactions were obtained in some nonsyphilitic diseases with the spirochetal antigens than with the lipoid antigens; however, in the leprosy group the incidence of false positive reactions was considerably lower with the spirochetal antigens than with the lipoid antigens. The increased specificity of spirochetal antigens has not been definitely established, and the occurrence of positive reactions with these antigens cannot be accepted as indicative of a syphilitic infection. Rein and Pillemer<sup>37</sup> found that fresh unheated serum inhibits or retards the aggregation of lipoidal antigens by the serums of syphilitics. Of greater interest was the finding that fresh serum had little or no effect on the aggregation of lipoidal antigens by the positive serums of horses and cows or the positive serums from nonsyphilitic individuals. Based on these findings, an "inhibition procedure" was devised with the belief that it might differentiate between true and false positive serological reactions for syphilis. Several thousand serums have been subjected to this experimental inhibition procedure. At first the results were exceptionally good and most encouraging. Before long, however, it was found that this method had definite limitations. The other verification, confirmation, and spirochetal complement-fixation tests also had limitations which rendered them unsatisfactory for practical use.

Neurath and his associates have made extensive studies<sup>25</sup> relating to the problem of biologic false positive reactions in serologic tests for syphilis and have developed a globulin-inhibition method for differentiating true from false positive reac-



tions. In a large series of carefully selected blood specimens, their method has been successful in distinguishing between these two types of reactions in about 95 per cent of the cases. This method is now under investigation in laboratories other than the originator, and it is hoped that it will give equally as good results.

Several methods have been developed for the differentiation of the true (syphilitic) serologic reactions from the false positive (nonsyphilitic) serologic reactions. None of these methods (except possibly for the globulin-inhibition method of Neurath) has been able to distinguish consistently between the true and false positive serologic reactions. There is need for such a procedure which is reliable, and investigation along these lines should be subjected to critical evaluation by independent workers before it is adopted as a routine procedure.

### Conclusions

1. Modern serodiagnostic tests for syphilis, employing purified antigens, are extremely valuable to the physician in establishing or excluding a syphilitic infection.

2. With improvement in techniques and materials employed, the specificity and sensitivity of the serodiagnostic procedure has been appreciably increased.

3. There are certain limitations (false negative and false positive reactions) inherent in the currently employed tests. The physician must be aware of these limitations, for otherwise serious errors of omission and commission will be made.

4. There is a great need for the development of a procedure which would consistently differentiate between true and false positive reactions.

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# Concept of Arterial Hypertension

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IN 1932, GOLDBLATT<sup>13</sup> and his collaborators reported the first of a series of experiments showing that partial constriction of the renal arteries of animals was followed by arterial hypertension. By means of a special clamp applied to the main renal arteries of dogs, monkeys, and rats, it was shown that by varying the degree of narrowing of the arterial lumen, thereby producing various degrees of renal ischemia, an arterial hypertension of the benign type with little or no renal functional disturbance, or of the malignant type with definite kidney damage, could be produced at will. These observations were shortly confirmed by numerous other investigators,<sup>11</sup> including Page,<sup>22</sup> who has done further extensive experimentation, including the observation that a definite hypertension is also produced when the kidney is surrounded by cellophane or silk, producing a perinephritis with a fibrous capsule, the removal of which relieves the hypertension.

The importance of these experimental findings as a step forward in our understanding of arterial hypertension was immediately recognized. They created a renewed widespread medical interest in a condition of previous obscure etiology, and stimulated a great increase of experimental and clinical observation. Earlier observers had shown that there was a relationship between kidney disease and vascular hypertension, but none had shown it so graphically. Richard Bright suspected such a relationship a century ago by observing that an enlarged heart was usually found with kidney disease. Other investigators in more recent years have also insisted on such a relationship.<sup>8</sup> A pressor substance extracted from the kidney many years previously escaped the attention which it deserved because a definite chemical amine could not be detected.<sup>20</sup>

From the Department of Internal Medicine, Harper Hospital, Detroit, Michigan. Read at a meeting of the Detroit Academy of Medicine, March, 1945.

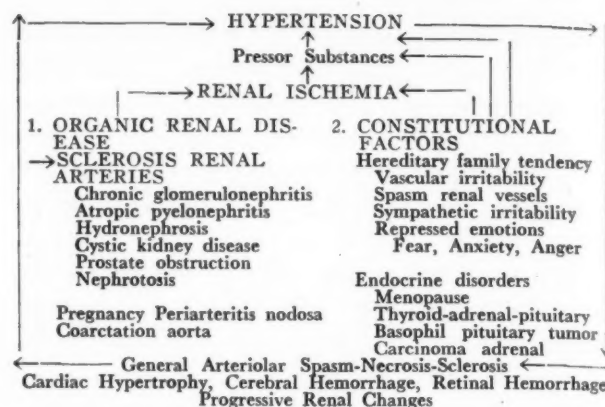


Diagram 1. The etiology of arterial hypertension as diagrammed above presupposes the existence originally of at least two factors, one constitutional, the other renal (pressor substances), which combine to produce a third factor, arteriolar sclerosis and narrowing, which in turn causes more hypertension and also more renal ischemia. A vicious circle is produced.

Not long after the experimental demonstration that renal ischemia produced hypertension, there began to appear clinical reports showing that at times, the surgical removal of a diseased kidney for a hypertensive patient led to a return to normal of the blood pressure. These reports seemed to prove that a unilateral diseased kidney may at times cause a definite arterial hypertension.

This discussion aims to present briefly the observations and viewpoints from the fields of experimental investigation, internal medicine and surgery and to present a concept of the mechanism of arterial hypertension. The opinions of Schroeder<sup>25</sup> regarding such a mechanism seem to conform best with demonstrated observations. It is probable that hypertension is rarely the result of a single factor, but is the result of two factors which cause a third similar factor to come into being. The relative severity of these different factors determine the progress and the severity of the disease.

## Mechanism of Arterial Hypertension

In Diagram 1, I have attempted to portray the concept of hypertension herein discussed. It shows that the following factors are at work in most cases of hypertension: (1) renal ischemia, (2) the production of pressor substances, (3) a constitutional nervous factor, and (4) the damaging effect of continued hypertension on the arterioles. A vicious circle is in effect.

1. *Renal ischemia* means a decreased flow of arterial blood through the kidneys. This may be due to a narrowing of the afferent arteries or arterioles by sclerotic changes or spasm. Arterioscle-

rotic changes in the renal vessels are thought to be the most common initiating factor, as seen in clinical arterial hypertension. Narrowing of the efferent arterioles may also cause a decreased total blood flow. Both of these conditions may be caused by numerous types of renal pathology.

Glomerulonephritis, both acute and chronic, has long been known to be frequently associated with hypertension, and the pathologic lesions found at post mortem suggest that renal ischemia may have been present. Chronic pyelonephritis, hydronephrosis, nephroptosis, polycystic kidney disease and urinary obstruction have been reported as causes of renal ischemia and hypertension. Cases of these conditions have been reported in which the surgical removal of such a unilateral diseased kidney was followed by a return of the blood pressure to normal.

Such surgical kidney disease is, however, but rarely a cause of arterial hypertension, as evidenced by the reports of Braasch, Walters and Hammer,<sup>4</sup> of Crabtree and Chaset,<sup>7</sup> of Schroeder and Fish,<sup>26</sup> and of Mulholland.<sup>19</sup> Of a large number of patients with surgical kidney disease, about the same percentage (20 per cent) had hypertension as is observed in any average group of adult patients. However, in the case of severe atrophic pyelonephritis, about 45 per cent showed hypertension, and removal of the infected kidney caused the blood pressure to return to normal in 70 per cent of those having hypertension before operation. Extensive renal and vascular sclerosis was present in all of the surgically removed atrophic pyelonephritis cases and yet only 40 per cent showed hypertension. It has been remarked, "It would seem that certain systemic factors exist in one individual which cause hypertension in the presence of a renal lesion, but that existence of the same renal factors does not affect the blood pressure in another individual."<sup>4</sup>

Hypertension occurs in approximately 15 per cent of all persons and in about 33 per cent of persons more than fifty years of age.<sup>16</sup> Therefore, the incidence of high blood pressure would be high in any group of persons suffering from renal or any other disease.

Arteriosclerotic plaques were found causing a reduction in the lumen of the main renal arteries in 86 per cent of fifty cases of essential hypertension, while control cases showed only 10 per cent with comparable lesions.<sup>3</sup>

An interesting explanation of the hypertension of pregnancy is given by Gabriele.<sup>10</sup> It is contend-

ed that the kidney is raised, especially late in pregnancy, thereby changing the piezometric angle of the renal arteries and causing a renal ischemia with the subsequent liberation of pressor substances.

Hypertension has been reported in cases of periarteritis nodosa in which the renal arteries were involved and ischemia resulted. Also in coarctation of the aorta, hypertension has been noted as a result of decreased renal blood flow.

2. *The Production of Pressor Substances.*—When the renal blood vessels are diminished in caliber, there is produced more of a slow, steady flow of blood rather than a pulsating one. The pulse pressure is lowered, the blood flow slows and there is a relative anoxia. Under these conditions of ischemia, renin, a protein present in the cortex of normal kidneys, is liberated into the general circulation. Renin itself is not a vasoconstrictor, but in the blood stream, it unites with a pseudoglobulin, forming a substance called angiotonin, which is a highly active vasoconstrictor of a special sort. Angiotonin causes a constriction of small arteries and arterioles and an augmented heart beat, thereby raising the blood pressure. It does not cause a closure of the capillaries with a decreased peripheral blood flow and paleness, as is the action of adrenalin and posterior pituitary extract. This is the explanation of Page.<sup>20</sup> Another explanation is that the kidneys contain an enzyme which oxidizes certain amines only in the presence of abundant oxygen, but when there is an ischemia and anoxia, many amines are formed and liberated which are marked pressor substances.

3. *The Constitutional Factors.*—There is a marked hereditary tendency towards hypertension in many families. About 80 per cent of hypertension cases show a family history of hypertension. Investigation has shown that children in these hypertension families often react excessively to tests of vascular irritability, and those that do have this vascular irritability are more apt to later develop high blood pressure.<sup>2</sup> By means of the Cold-Pressor Test,<sup>17</sup> abnormal vasolability can be detected before the appearance of high blood pressure. There has been found some practical prophylactic value in the early detection of such cases.<sup>30</sup>

It has previously been mentioned that among people having the same degree of pyelonephritis and renal sclerosis in their surgically removed kid-



ney, studied pathologically, some develop hypertension while others don't.

Individuals who have hypertension are apt to have a high-strung, excitable emotional disposition and a build of the sthenic, stocky, short-necked type.

From an experimental standpoint, it has been found that constriction of the blood flow of one kidney in rats usually causes hypertension and often renal arteriolar necrosis, while in dogs it is usually necessary to produce ischemia in both kidneys in order to produce these changes. Only the excitable, nervous dog will respond to a lesion of one kidney alone.

Physicians are familiar with the marked, though transient, effect of the emotions of anxiety and anger on the blood pressure of many patients. The blood pressure is often high when taken by a new doctor in a strange office. I have seen it very high in patients who were worried because a doctor had recently found a high blood pressure and had left them with the impression that there was little or no treatment for the condition. The pressure may fall and the patients show much subjective improvement when they feel that their condition is understood and is being correctly treated by a new doctor.

The statement that "every psychic tendency seeks adequate bodily expression"<sup>21</sup> should be kept in mind in considering a hypertension patient. Inner tension, fear, or anger, which cannot be released through ordinary channels (action or words) may manifest itself in the vascular system.

The splanchnic sympathetic nerves are important in maintaining a normal or elevated blood pressure. When all of them are cut preganglionically, an elevated blood pressure is often reduced. Sympathectomy does not, however, according to experiments, cause an increased renal blood flow. Page<sup>21</sup> states that "A better explanation appears to be that the decrease of arterial pressure which follows sympathectomy in man is an expression of denervation of the reactive visceral splanchnic innervation with resultant partial failure of venous return most evident in the erect posture. The decrease of venous return limits cardiac output and thus tends to decrease arterial pressure."

Vasoconstriction of the renal vessels and ischemia can be produced by anxiety<sup>28</sup> as well as by direct stimulation of the sympathetics<sup>5</sup> and also by injections of adrenalin.<sup>24</sup> Prolonged arterial hypertension has not been produced by any of these

methods,<sup>9</sup> yet it is possible that repeated psychic trauma, or prolonged repressed anxiety or anger in people predisposed by heredity, might produce enough renal vascular spasm and ischemia to become a permanent change.

Experimentally, injection of kaolin into the cisterna magna and also section of the inhibitory sino-aortic nerves produces a lasting hypertension, which is relieved by complete sympathectomy.<sup>6</sup>

Basophile tumors of the pituitary gland and some carcinomata of the adrenal produce a lasting arterial hypertension, which if prolonged, may show the resultant renal arteriosclerosis.

In experimental hypertensive animals, removal of the pituitary lowers the blood pressure. The same is true if both adrenals are removed when adequate doses of sodium chloride and adrenal cortex extract are given. Removal of one adrenal and only the medulla of the other does not alter the blood pressure. Thyroidectomy and gonadectomy are without effect on hypertension in humans.

The conclusion seems to be that the adrenal cortex maintains the vascular tree in a state receptive to vasoconstrictor substances, such as angiotonin, but does not participate in the mechanism itself. The same applies to the role played by the nervous system.

4. *The Damaging Effect of Hypertension on the Vascular System.*—Elevation of the arterial tension is the result of a stimulus which causes constriction of the small arteries and arterioles and simultaneously, an augmentation of the heart beat. Angiotonin has these same pharmacologic effects. As the hypertensive process continues, the arteriolar spasm leads to a arteriolar muscle hypertrophy. The cells increase in size until they exceed the limits of efficient diffusion of nutriment into them and there ensues a necrotizing arteriolitis with fibrosis and sclerosis and a permanent narrowing of the arteriolar bed. The augmentation of the heart beat leads to cardiac hypertrophy and sclerosis.

General arteriosclerosis of the larger arteries is an entirely different entity with a different pathological and clinical picture. The sclerosis is in the intima of the larger arteries and not media of the arterioles.

As hypertensive arterial disease progresses, it becomes more and more manifested by cardiac hypertrophy and sclerosis, with clinical, x-ray, and electrocardiographic changes; by retinal hemorrhages and papilledemia; by progressive renal

changes, with urinary blood cells, casts and albumin; and by sclerosis in the cerebrum and other vital organs.

A situation is found in the kidneys which may not only be the effect of hypertension but may also cause hypertension—a vicious circle.

Experimental evidence supports this relation. Dogs, when subjected to bilateral renal ischemia and the resulting hypertension, develop arteriolar necrosis and sclerosis in other organs.<sup>12</sup> Rats rendered hypertensive by ischemia in one kidney develop the same lesions in the other kidney and other organs.<sup>27</sup>

Pathological examination has shown sclerosis of the afferent kidney vessels in all cases<sup>18</sup>, and of the efferent kidney vessels in most cases<sup>14</sup>, of arterial hypertension cases at autopsy.

*Résumé of Arterial Hypertension Mechanism.*—Two factors are necessary in the production of a persistent high blood pressure: (1) a constitutional vascular irritability or spasm tendency, and (2) renal ischemia. Each may cause the other, producing a vicious circle. Briefly stated, in individuals predisposed by constitutional nervous or endocrine vasospasm tendencies, the development of renal vessel sclerosis and renal ischemia, with the liberation of pressor substances, produces an accentuation of the vascular spasm and a continuous arterial hypertension. This hypertension by itself causes spasm, hypertrophy, narrowing and sclerosis of the terminal arterioles, including those of the kidney, and an irreversible vicious circle is produced. In the great majority of patients the vascular spasm factor initiates the disorder, but, occasionally the renal lesion is primary.

### Management of Hypertension

Arterial hypertension can be controlled and its progress retarded in the great majority of patients, thereby giving such people many years of useful life.

A. Investigate carefully the possibility of the patient having a unilateral surgical kidney. This condition is rare as a cause of hypertension but it does exist occasionally.

B. Utilize all therapeutic measures which promote vascular relaxation, including rest, physical therapy, diet, medicines, psychotherapy and surgery.

1. *Rest.*—Most patients with hypertension are ambitious, responsible, forceful and high strung. They do not enjoy rest and relaxation. It is therefore often very difficult to impress upon the patient the necessity of such a method of living. They should be instructed to get ten hours in bed every night and one or two hours after the noon meal if possible. They should take vacations several times per year, and avoid fatigue especially.

2. *Physical therapy.*—A warm salt bath at bedtime generally is relaxing. Sweat baths and massage are good for the obese. Moderate exercise, such as golf and walking, is indicated if there is no cardiac failure.

3. *The diet* should be balanced in carbohydrate, protein, fat, minerals, and vitamins, with calories sufficient to reach or maintain the ideal weight for the patient. Reduction of the weight is advisable for those overweight. A very low protein diet for one or two months often helps in reduction of blood pressure, especially if the patient has previously been on too great a protein intake. Tobacco should be eliminated entirely. Alcohol in moderate doses is advisable for its relaxing effect. Coffee and tea should be limited to one or two cups per day. Water intake should be two to three quarts daily.

4. *Medicines.*—No one drug has been found to be the best in the control of hypertension. Several drugs and combination of drugs have been found to be of value when given careful control and observation.

(a) Sedatives may be given in adequate dosage for relaxation but not to interfere with cerebral activities. Any of the barbiturates may be used but the type of sedatives should be changed every month or so in order to avoid toxic action. Bromides are of value for periods of one or two weeks every one or two months. Whisky, one or two ounces after noon and night meals, is useful. Aspirin with codein is very relaxing during nervous or headache spells.

(b) Vasodilators: Manitol-hexanitrate after meals and at bedtime, especially in combination with a small amount of phenobarbital, will usually keep a blood pressure down within safe limits. Sulfocyanates in proper dosage will control blood pressure in about 50 per cent of cases. The blood cyanate level should be checked every few weeks.

When this precaution has been taken I have never seen any bad effect from the drug. Xanthine derivatives act chiefly on the coronary and kidney blood flow. Aminophyllin, theobromin, and theocalcin are the drugs most used.

(c) Iodides are of little direct value except in the cases of mild hyperthyroidism.

(d) Estrone is of value if the menopause is a factor in pathogenesis, and testosterone may be of aid for the male.

5. *Psychotherapy*.—Liberal doses of optimism and encouragement should be given. The patient should be instructed and made to avoid all unnecessary strains, stresses and worries of life. This is now called by the psychiatrist "preventive psychiatry." The patient should develop a philosophy of life which "lets the other fellow worry," or "it will not matter much 100 years from now."

6. *Sympathectomy*.—This procedure, while a formidable operation, will often prolong a patient's life in comfort for many years. It is especially indicated in those cases of malignant hypertension which do not respond to the medical measures previously outlined. The operation should be done before too much damage has been done to the arterioles by the hypertension. Peet<sup>23</sup>, Southwick<sup>29</sup>, and Grimson<sup>15</sup> have been the greatest exponents of this form of treatment.

### Summary

A concept of arterial hypertension is presented which presupposes a constitutional, probably hereditary, vascular sympathetic nervous irritability, which causes, or on which is superimposed, a renal ischemia. The combination of the two produces the vicious circle of arterial hypertension. Essential hypertension is a name given to an early stage of this condition before the renal ischemia has become very manifest by clinical tests. Malignant hypertension is a rapidly developing uncontrollable case. Treatment seldom cures, but generally it is able to control the progress of the disorder and prolong life in comparative comfort. The management of hypertension is outlined. Its value might be compared to the use of liver extract in primary anemia, or glasses in vision trouble.

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### STOP—LOOK—LISTEN

STOP telling the patient there is nothing wrong with him but nerves—Don't say: Go home and forget it. LOOK for the facts as the patient sees them. LISTEN attentively to patient's story.

\* \* \*

The patient who is always tired is more liable to be suffering from emotional fatigue than from anemia or avitaminosis.

\* \* \*

The most valuable thing in the treatment of a nervous, emotionally disturbed patient is to have security—not to the point of too great dependency.

\* \* \*

You can't treat the emotional problems in your own family.

\* \* \*

Seventy-five per cent to 80 per cent of organic illnesses have unhealthy psychic components.

\* \* \*

Psychosomatic symptoms arise from being unable to solve emotional conflicts arising from disturbing situations. These conflicts may be recent but in many cases are of remote origin.

MICHIGAN MENTAL HYGIENE COMMITTEE

JOUR. MSMS



# Gynecological and Obstetrical Problems of the Industrial Physician

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THE PRESENT-DAY industrial physician is charged with the responsibility of inaugurating health maintenance programs which will aid in the reduction of lost time resulting from illness. That such programs should be the chief concern of those physicians specializing in this field of medicine

is proven by the fact that the larger corporations who keep accurate records of sick absenteeism report that of every 100 days lost by the employee from illness or accident, only six of these days can be charged to an occupational cause; ninety-four of the 100 days lost are the result of *non-occupational* illness or accident.

Until recently, these health maintenance programs have been concerned mainly with such obviously disabling diseases as tuberculosis, syphilis, the common cold, digestive diseases, malnutrition, nervous and mental disorders, cardiovascular-renal disease, et cetera. With the enormous increase in the number of women employed during the war years, and at present with their largest peacetime employment, an added responsibility comes to the industrial physician—the establishment of a health maintenance program that will aid in the reduction of sick absenteeism resulting from illness peculiar to this group.

The problems that women bring to industry cannot be dismissed by stating that there are no widespread occupational diseases peculiar to women, nor that the high absenteeism rates of female employees are the result of their attempt at carrying on two jobs—the one in the factory, the other in maintaining the home.

In a recent study made by a large industry operating in thirty-six states, the disability rate for

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female employees was 292 per 1,000. These statistics covered illnesses lasting longer than one week. Gynecological disease, including acute appendicitis, accounted for 26 per cent of that total. During this same period, pregnancy was responsible for an absenteeism rate of forty-five per 1,000.

The industrial physician has found that the gynecological conditions most frequently brought to his attention and most commonly associated by the employee with her work are low back pain, dysmenorrhea, amenorrhea, excessive or intermenstrual bleeding, pelvic pain, the aggravation of symptoms of the menopause and pelvic relaxations (cystocele, rectocele and prolapse of the uterus).

What are his responsibilities in these cases, and what can he do in outlining a health maintenance program that will aid in their solution?

## Pre-employment Gynecological Considerations

During the pre-employment physical examination, a knowledge of the previous health of the prospective employee is basic in evaluating the ability of that individual to do safely the job to which she has been assigned. It is of extreme importance to know whether there have been disabilities arising from dysmenorrhea, pelvic pain, repeated abortions, excessive menstrual flow or intermenstrual bleeding, et cetera. It is just as basic that a pelvic examination should follow in the completion of such an evaluation.

X-ray of the chest, visual acuity tests, blood pressure readings, urine examinations and serological tests have become standard procedures in the pre-employment examination. Knowledge of any pathological state of the employee's pelvic organs is just as significant.

The importance of such knowledge becomes apparent when we study the trend of legislation relative to compensable occupational disease. Today, many of our state laws make little, if any, distinction between the liability of the employer in cases of disability arising directly out of employment, or such liability being the result of an aggravation of a pre-existing pathological state.

The prospective employee should be informed that the pre-employment examination is for the purpose of safe placement at work. It has been our experience that she readily accepts any examination that serves to protect her against disability or the aggravation of an already existing disease. Knowledge of past gynecological or obstetrical

pathologic condition, along with pelvic examination, is a fundamental inclusion in adequate health maintenance programs for the industrially employed female worker.

#### Gynecological Problems of Established Employee

Definite gynecological disease arising solely from an occupational cause is rare. Aggravation of a previously existing condition is common, and gynecological symptoms that the employee attributes to her work are legion.

*Dysmenorrhea*—The problem of dysmenorrhea is one that has caused the industrial physician much concern—concern often to the point of exasperation. His experience differs radically from that of the gynecologist in the approach to a solution of this problem.

First, he finds an attitude of resignation to this periodic disability which is amazing—resignation to such a degree that it has rarely occurred to them to seek medical advice. In our series, less than 12 per cent of those absenting themselves from one to three days each month, had ever requested an examination by their family physician.

Secondly, the discomfort of menstruation has previously furnished a large percentage of young women with an excuse to stay home from school or the avoidance of any unpleasant tasks. This attitude is carried into their factory environment where, with the mere mention of abdominal cramps, they expect leave with no questions asked.

Lastly, "epidemic dysmenorrhea" may be unknown to the gynecologist, but it has frequently been observed by the industrial physician. The transfer of *one* young woman to a different type of employment, when it was thought that the work she was doing was aggravating her symptoms, may bring many requests from other employees who seek similar changes, claiming similar disability.

What must the industrial physician include in his program of health maintenance that will tend to lessen the lost time from this source?

Wards should be provided in the industrial hospital where immediate relief can be obtained. The employee should *not* be sent home. Rest, local heat and simple medication soon return most of them to their work. However, it is during the intermenstrual period that the most beneficial results can be obtained. A sincere attempt should be made to correct the mental attitude of the employee. Correction of improper posture at work,

resulting in poor muscle tone, often necessitates change or rearrangement in her job. The importance of proper diet and the avoidance of constipation should be emphasized. Frequently, systematic exercises are outlined and outdoor activities encouraged.

By following such a program, one industrial institution employing over 9,000 women, reduced the lost time from dysmenorrhea approximately 75 per cent.

The industrial physician is responsible for the correction of conditions within the factory which cause abnormal changes in the congestive states of the menstrual cycle. It is not always the female employee who is on her feet all day, moving about before her machine, nor the one who is required to use her feet constantly in the operation of her job, who complains of dysmenorrhea. The women on the assembly lines, inspectors or clerks, who sit at tables or desks, find that these more sedentary occupations similarly cause alterations in their menstrual symptoms.

It is the industrial physician who must decide whether the employee should be relieved of strenuous tasks; advised to seek systematic exercise, or receive instruction in the physiology of menstruation that might result in a change in mental attitude towards this too often misunderstood normal function.

His must be a practical approach to this subject, for his ultimate goal is, after all, a type of health maintenance that reduces absenteeism and lessens disruption in production from this or any other periodic or repeated disability.

Finally, the industrial physician must always keep in mind that dysmenorrhea is but a symptom resulting from many conditions (pelvic inflammatory states, endometriosis, pelvic neoplasm, cervical stenosis, hormonal imbalance, et cetera) having nothing to do with employment. Such cases can best be treated by the employee's own personal physician.

*Abnormal Menstrual Flow and Inter-menstrual Bleeding*—The medical departments of our manufacturing institutions, functioning as "fact finding" agencies, have an unequalled opportunity for the recognition of early gynecological disease. Abnormal menstrual flow and inter-menstrual bleeding associated with ectopic pregnancy, threatened abortion, benign or malignant polyps, adenomyoma of the uterus, cervical cancer, et cetera, are fre-

quently first observed in those departments. When it is recognized that there is no occupational explanation for these symptoms, the insistence upon prompt medical attention has resulted not only in shortening the period of disability, but frequently has saved the life of the employe.

The diagnosis of early pulmonary tuberculosis in those industrially employed has been a recognized factor in the reduction of the death rate from that source. In the case of cervical cancer, especially, a similar service may be rendered by the industrial physician.

One cause of excessive menstruation or intermenstrual bleeding is of particular interest to the industrial physician. It has been noted that female employes working with certain chemicals, such as trichlorethylene, benzol, carbon disulfide, T.N.T. and lead, occasionally give symptoms of increased menstrual flow or "spotting" between their periods. The question immediately arises as to whether these chemicals have specific effects upon the female reproductive organs or whether their symptoms are merely manifestations of low grade toxic absorption resulting in hemorrhagic condition of the mucous membranes in any part of the body. In the case of lead, it is believed that there is a definite effect upon the reproductive function and the menstrual cycle.

The industrial physician's responsibility in this instance is to see that female employes are properly protected from such exposures.

*Pelvic Pain and Low Backache*—These symptoms have been grouped together, for they are commonly associated in the minds of the female industrial worker. The industrial physician again finds himself in an unenviable position, for, even when the employe knows that she has an existing pathologic condition, she only too frequently claims that her job is solely responsible for her symptoms.

A decision must be made at once. Is the basis for her complaint an inflammatory disease, cyst of the ovary, uterine fibroid, endometriosis, et cetera, or do these symptoms actually arise from lumbosacral strain, excessive fatigue, or bad posture at work? Pelvic examination is as essential, in these cases, as x-ray examination of the chest when pulmonary complications may be suspected.

When the industrial physician finds that a definite pelvic pathologic condition is present, it is his duty to see that these employes consult their family physician as to proper treatment.

*Pelvic Relaxations*—With the increased employment of older parous women in our industries, the problem of pelvic relaxations and their aggravation by certain types of work must be studied. Constant jarring, found in some riveting operations, heavy lifting, repeated uses of the feet in working certain power machines, or the requirement of standing long hours at a time, certainly aggravate the symptoms arising from cystocele, rectocele or a prolapsed uterus.

Actually these women should not be employed at this type of work. Transfer to lighter employment is one solution. When this is impossible, the industrial physician should see that these women be given sufficient rest periods to avoid excessive fatigue. Certainly it is his duty to examine the employe at frequent enough intervals to know whether her condition is becoming worse in spite of any change in occupation he may have insisted upon.

The male employe with hernia is given every attention. The problem of pelvic relaxation in the female must receive equal consideration.

*Menopause*—The menopause, with its associated nervous and vasomotor instability, increased excitability and susceptibility to fatigue, along with frequent attacks of vertigo, limits the type of work that these female employes should be allowed to do.

It is the responsibility of the industrial physician to recognize menopausal symptoms, see that proper medical care is instituted by the employe's own physician, and insist that she be placed at tasks requiring less nervous energy and concentration. Sympathetic understanding on the part of the industrial physician goes far in lessening lost time during this trying period.

*Pregnancy*—No phase of health maintenance for women in industry has received as much attention as that concerning pregnancy. The main problems involved are: should the employe continue at work once the diagnosis of pregnancy is established; under what circumstances should she be allowed to continue, and, if allowed to remain, what particular types of employment are safe, and what toxic exposures must be particularly guarded against.

State laws on this subject are few and inadequate. But four states (Massachusetts, Connecticut, Vermont and Missouri) legalize the length of



time the pregnant employe may remain at work, while only six (Washington, Connecticut, Massachusetts, New York, Vermont and Missouri) specifically state when she may be legally returned to work following the birth of her baby.

The industrial physician receives little guidance from this source. For example, a woman may, legally at least, be kept at work in Massachusetts or Vermont until two weeks before the estimated date of delivery, while in Connecticut, New York or Massachusetts she may be employed four weeks post partum, and in Missouri it is legal to place her at work in three weeks.

Fortunately, specific recommendations concerning pregnancy in the industrial female worker, have been prepared by the Children's Bureau, the Women's Bureau of the U. S. Department of Labor, and the Committee on Health of Women in Industry of the American Medical Association. These recommendations have been of great assistance to the industrial physician in formulating policies adaptable to the particular type of industry he serves.

A summary of these recommendations follows:

1. The labor situation in this country does not necessitate the recruitment or employment of pregnant women.

2. The employe, upon realizing that she is pregnant, should be urged to report her condition immediately to the industrial medical department, the Girls' Counselor, or to the superintendent of her department, so that transfer to lighter or less fatiguing work may result.

3. There should be no exposures to toxic substances considered to be extra hazardous during pregnancy, such as analine, benzol, toluol, carbon disulphide, carbon monoxide, chlorinated hydrocarbons, lead, mercury, nitrobenzol, phosphorus, radioactive substances or any other toxic substances that exert an injurious effect upon the blood-forming organs, the liver, or the kidneys.

4. Facilities for adequate pre-natal medical care should be readily available for all employed pregnant women; they should be instructed as to the importance of much care. Many industrial institutions require a note from the family physician stating that pre-natal care has been instituted before the employe is allowed to continue at work.

5. A minimum of six weeks' leave before delivery should be granted. (The word "minimum"

should be emphasized, for in many occupations employment beyond the six-month period is extremely hazardous.) It might be added that, where there is a previous history of repeated abortions, severe toxemias, existent pyelitis, kidney or heart disease, serious varicosities or sacro-iliac difficulties, the employe should be placed on a medical leave of absence, and the industrial physician should furnish the obstetrician with any data he may have accumulated concerning this individual, such as reports of urine analyses, blood pressure readings, blood tests, x-ray findings, et cetera.

As the disability rates for premature termination of pregnancy are rising, closer co-operation between the industrial physician and the obstetrician is mandatory.

6. It is recommended that, in uncomplicated cases, a period of six weeks should follow delivery before the new mother should be returned to work. (Here again, that this is a "minimum" period should be given emphasis.)

This last recommendation is one which causes the industrial physician considerable apprehension. The Unemployment Compensation Commission Act complicates the decision he has to make.

At the time of the final postpartum examination, the employe requests a statement from her physician that she now is able to return to work. She then goes before the commission, using this note to establish that she "is able and available for her previous position." This being established with the commission, she is referred to her former employer.

At this point, the industrial physician is in difficulties. If he is hesitant about placing the employe at work, feeling that her job at the factory and her added responsibilities at home are more than she is physically capable of doing without damage to her health, she then is entitled to unemployment benefits. If he indiscriminately approves these new mothers for return to work, using the family physician's note as his authority, he is certainly not forwarding his health maintenance program.

This is but another instance where a better mutual understanding of the problems of the industrial physician and the family physician would benefit both and the employe as well.

### Conclusion

The industrial physician's consideration of gynecological and obstetrical problems is but a part of

(Continued on Page 605)

# Tumors of the Female Breast

## A Diagnostic and Therapeutic Summary

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and

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R. D. McClure

UNDOUBTEDLY, no discussion of a disease that claims, as breast cancer does, over 16,000 lives yearly,<sup>30</sup> can be considered untimely or trite. What makes it, however, even more proper to return again and again to a review of our knowledge of the new-growths of the breast is the circumstance that practically all this enormous loss of life is preventable. The opportunity is rare where one can uncover a neoplasm as early as in the breast, and it is precisely in early detection that our hope of a greater saving of lives rests. The rate of early diagnosis will increase proportionately as our patients learn to seek medical advice about any lump discovered in the breast and as we physicians, ourselves, learn to look upon any such lesion with the seriousness it rightfully demands. This is to say that we shall do our duty in full only if we regard the diagnosis of any swelling in the female breast as the differential diagnosis of breast cancer. Some of the cardinal points of this differential diagnosis form the theme of this brief discourse.

### Methods of Examination

The minutiae of physical examination are too well known to be discussed here. One must stress, however, even at the risk of sounding elementary, the importance of thoroughness in the examination of the breasts of all the female patients who, for any reason, present themselves for general physical examination. The discovery of an early breast cancer during a routine physical examination is nothing short of an act of life saving; it is one of the gratifying rewards of our profession. Its oversight is a disaster we can hardly excuse. One may also mention that a too vigorous search of the axilla for lymphnode enlargement is not to be recommended in a case of suspected cancer. The margin

of error is great<sup>13</sup> and the danger of traumatizing a cancer-bearing gland is real.

One may advantageously resort in the investigation of a breast tumor to transillumination in a darkroom. This method often yields information about the density and configuration of a tumor. Aspiration, likewise, is useful in determining the nature of a suspected cyst. Radiography after the injection of an opaque material—so-called galactography—has been advocated by some but this method has found little general acceptance.

### General Principle of Procedure

As it has just been mentioned, our attitude in the presence of a tumor of the breast must be that of suspicion, that of suspecting carcinoma until convinced otherwise. There is only one dependable means of being convinced: the microscopic report of the pathologist. Thus, all tumors of the breast must be excised for biopsy. We have long followed the practice of doing these biopsies with the full preparation for a possible radical operation, the details of which will be outlined presently. We shall first review, however, very briefly the commonest lesions that call for biopsy, indicating at the same time their definitive treatment.

### Inflammatory and Traumatic Swellings

Among the pyogenic infections of the breast, the diffuse phlegmonous type may at times raise the problem of differentiation from a rapidly growing and highly malignant carcinoma. Thick-walled chronic pyogenic abscesses may cause a similar difficulty. Both instances are rare and the biopsy will decide the diagnosis. A therapeutic test with penicillin may be helpful.

The circumscribed, nonsuppurative forms of specific granulomas, especially the proliferative type of tuberculosis, occasionally are impossible to distinguish from malignant neoplasm grossly. Biopsy is essential for the diagnosis. Generally a simple mastectomy is the treatment.

Trauma to the breast may lead to tumor formation by causing focal necrosis of the adipose tissue. The necrotized fat may liquefy and result in a pseudo-cyst, or it may become fibrotic and form a nodule whose fixed and hard character may easily remind one of cancer. These nodules and false cysts may best be removed, unless their origin is obvious. It may be added that, besides the ordinary hematoma, the traumatic cyst and

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nodule are the only breast lesions which can rightfully be attributed to the effect of injury, although many a patient with breast cancer is wont to trace her trouble to a blow or similar trauma.

### Hormones and the Female Breast

In an evaluation of the next group of breast tumors, the true neoplasms, an understanding of the factors governing mammary development is helpful.<sup>24</sup>

As a physiological division of the female reproductive system, the breast is subject to the same hormonal stimuli as the other tissues serving the purposes of reproduction. The estrogens have a growth-promoting effect on the duct system and perhaps, also, on the periductile connective tissue. In combination with the estrogens, the secretion of the corpus luteum, progesterin, stimulates alveolar and lobular development. In addition to the ovarian hormones, pituitary secretions have also been found necessary for the normal development of mammary tissue and for the secretion of milk (lactogenic hormone or prolactin).

Numerous experimental and clinical observations have been made that suggest that neoplasms of the breast have an etiologic relationship to the state of balance of the hormonal factors acting upon the functioning breast tissue. Some of these will be indicated presently. It should be stressed, however, that much of our concept of this hormonal mechanism is speculative.

### Fibroadenoma

This discrete, usually single, freely movable and ovoid or spherical tumor is the commonest surgical lesion of the breast of the woman in the third and fourth decades of life. When cut grossly, its surface is grayish-white and somewhat rubbery, with darker and slightly raised foci scattered through it. The latter represent the glandular elements in the fibrous bulk of the tumor. A well-circumscribed capsule is present, and the tumor shells out easily at operation. Fibroadenomas probably represent a localized response to the normal hormonal stimulation to which the breast is subject. There seems to be a predisposition for sarcoma to develop in fibroadenomas, but it is questionable that carcinoma may arise from this neoplasm.<sup>33</sup> The treatment is local surgical excision.

### Fibrocystic Disease (Chronic Cystic Mastitis)

This pathological complex comprises a varied group of neoplastic changes<sup>3,5-7,17,27,32</sup> and is the

breast lesion most commonly seen in surgical clinics. It is likewise the lesion that poses the most trying questions of differential diagnosis and management.

It simplifies the understanding of this disease if one conceives of its various forms as quantitatively different combinations of certain qualitatively similar pathologic changes. These changes are essentially as follows: proliferation of the acinar epithelium, dilatation of the duct system with or without epithelial hyperplasia and with or without cyst formation, hyperplasia of the connective tissue elements, and focal lymphocytic infiltrations (the latter feature having given ground for the name of chronic mastitis, even though the disease is not an inflammatory one). These alterations occur in varying combinations and proportions, now the epithelial proliferation predominating, now the fibrosis being more pronounced, then again the cyst formation being the most marked. For practical considerations, the forms with epithelial hyperplasia are the most important ones since these may represent precancerous lesions. Unfortunately, clinically the differentiation of one form from another is usually impossible. In general, they present a rather diffuse "lumpiness," the glandular substance of the breast being irregularly thickened and somewhat rubbery and worm-like; discrete condensations of tissue that may be cystic or firm (in the latter case very closely resembling cancer), and also frank cysts, are often palpable. It is the circumscribed nodule that, as a rule, brings the patient to the surgeon. The disease involves the entire mammary gland and is almost invariably bilateral, although there may be a marked difference in the degree of involvement between the two sides and in the various segments of the same breast.

The entities called *adenofibrosis*, *chronic mastitis* and *cyclic hyperplasia* may best be regarded as graded phases of the general picture of fibrocystic disease.

In the causation of all the forms of fibrocystic disease, a hormonal factor plays a definite role. In the fully developed form, one very likely deals with a prolonged estrogenic stimulation without the necessary counterbalance of the corpus luteum hormone. A striking clinical feature of the more advanced disease is its prevalence in nulliparous women and in the postmenopausal age group.

The great practical importance of chronic cystic mastitis lies in its relationship to the develop-



ment of carcinoma. The opinions are not yet unanimous, and the evidence is complex and somewhat confusing.<sup>3,5-7,17,27,32</sup> Some practical facts may, however, be profitably pointed out. There is no doubt, for instance, that a certain number of breasts with fibrocystic disease contain areas of epithelial hyperplasia that are actually or potentially precancerous. One even encounters foci of changes that are microscopically malignant. Moreover, clinically these breasts are usually indistinguishable from those that have no malignant potentialities. On the other hand, the proportion of breasts with fibrocystic disease that carry the danger of malignant change is not sufficiently great to warrant surgery of the more radical type (simple or radical mastectomy) as a routine treatment of the disease. With these considerations in mind, one is able to outline a method of management that will combine a justified conservatism with a cautious regard for the possible risks.

In all cases that show the characteristic diffuse changes without a localized mass or nodule, repeated observations at three- or six-month intervals are advised. When a palpable mass is found, its prompt removal for biopsy is urged. If the lesion on frozen section is reported benign, no further surgery is done. In case the microscopic picture discloses hyperplasia of precancerous potentiality, and particularly if this occurs in a woman over fifty, a simple mastectomy is performed. If a benign nodule recurs, usually simple mastectomy is advised. In the latter case, however, the patient's age and her attitude toward losing her breast are considerations that may influence one to prefer repeated excision to simple mastectomy. Unless there are definite local changes in the opposite breast, which are judged on their own merits, we do not perform bilateral mastectomies for fibrocystic disease.

We do not believe that hormone therapy has a useful place in the management of chronic cystic mastitis.

#### Bleeding Nipple

This often troublesome problem<sup>4,31</sup> may be briefly mentioned here since it is usually caused by an intraductile papilloma or papillomata, and this lesion, in turn, is often a part of the complex picture of fibrocystic disease. When bleeding from the nipple is associated with a palpable and discrete mass, biopsy, excision and (if the frozen section warrants) radical mastectomy are done. If

the typical clinical picture of fibrocystic disease is present, the criteria of management are the same as those for that disease. Bleeding without cystic disease and without a palpable mass is treated with periodic observation.

#### Cancer of the Breast

We shall not discuss the pathological and clinical aspects of breast cancer<sup>20-23,25</sup> but shall limit these remarks to a summary of the methods of treatment used in our hospital. As regards the clinical features of carcinoma of the breast, it is earnestly to be hoped that they will soon become obsolete and that we shall see our patients with breast cancer so early in their disease that their diagnosis will depend entirely on the pathologist's report.

To assign the proper value to certain of the therapeutic measures in the management of breast cancer, it will be useful to cast a quick glance at some of the recent results of cancer research.<sup>15,29</sup> Much of the most fruitful work in this field has been done on carcinoma of the breast in mice. The essential importance of genetic susceptibility has been established beyond reasonable doubt. A very striking new discovery has been the recognition of a factor, transmitted through the milk of the mother, that is necessary for the appearance of breast cancer in mice. This milk factor has many of the characteristics of a virus. Finally, it has been shown that the presence of estrogenic hormones is essential for the development of carcinoma of the breast in these animals.

It is inviting to translate these experiments into speculations about human cancer. A great deal of caution must, however, be exercised in any such attempt. The results of the animal experimenter are stimulating and useful in guiding the interests of the clinician toward promising lines of thought; it is a mistake, however, to transfer these results directly to human therapeutics. It is particularly important to remember that there is no reliable evidence that hormonal stimuli are the direct cause of malignant change in the human breast. Nor is there justification in advocating that, on the grounds of the experimental work with the milk factor, all women with a family history, however remote, of cancer should not nurse their infants.<sup>11,18</sup>

As to our criteria of operability of cancer of the breast, they can be stated simply. We advise radical removal of all breast cancer that does not have

distant metastases and that is not fixed to the chest wall.

The steps in our preoperative preparation are essentially the same for all breast biopsies regardless of the weight of evidence for or against carcinoma. The responsible relative of the patient is acquainted with the facts and possibilities of the case. It is he and not the patient who is told about the chances of a malignant tumor being present and the implications of this possibility. It is sufficient simply to point out the possible need for the removal of the breast. Operative technicalities to a layman are superfluous and often disturbing. Some general anesthetic agent is used and the patient is draped with the expectation that a radical operation may have to be done. Arrangements are made for blood transfusion during and after operation and for skin grafting. A pathologist is available for the rendering of a diagnosis on the frozen section of the removed tissue. The definitive form of treatment is not decided upon until the pathologist's report is on hand.

We have used exclusively the Halsted type of radical mastectomy in the treatment of breast cancer. We are quite convinced that none of the cardinal principles of this operation can be violated without the penalty of a lessened chance of cure. A wide skin incision that almost invariably requires skin grafting for closure; extensive dissection of the skin flaps close to the dermis; removal *en bloc* of the pectoralis major and minor muscles, of the sheath of the axillary vein, of the axillary content, and of the upper rectus sheath: all these are indispensable steps for the eradication of the carcinoma.

There is some disagreement as to the timing and effectiveness of x-ray irradiation.<sup>10,16</sup> Statistically, the advantages of irradiation in cases without axillary metastases are questionable.<sup>13</sup> Since, however, it is well established that metastatic spread is favorably influenced, and since no operation, however thorough, can claim to extirpate all the possible regional nests of cancer cells, the continued use of irradiation seems logical. We recommend irradiation in all cases of breast cancer, and we prefer to give the treatment postoperatively, starting the series as soon as the wound is healed.

In the past, inoperable cancer of the breast was treated with irradiation and possibly with a simple removal of an ulcerated neoplastic mass if such was present. Recently, hormonal therapy has

been tried on the assumption that the estrogenic hormones of the ovary are cancerogenous. Two lines of attack have been evolved: (1) the disruption of the production of estrogens by castration either with the knife or with x-ray irradiation,<sup>12,14,26</sup> and (2) the neutralizing of these hormones by the administration of testosterone or allied substances.<sup>2,8,28</sup> Unquestionably, good alleviation can be obtained by either method. We have used testosterone propionate in conjunction with irradiation in a few cases and noted satisfactory response but only temporarily. The general trend of the results in published reports seems to be similar.

It may be mentioned that the artificial disruption of ovarian function has been tried out also as a routine auxiliary measure with radical surgery regardless of the state of advancement of the primary tumor.<sup>14</sup> The advantages of this audacious therapeutic step are not easy to see.

Before closing this brief review, we wish to mention that we consider *Paget's disease* as a true malignant neoplasm and treat it as such. A word should be said, also, regarding sarcomas of the breast.<sup>1,9,19</sup> These are rare tumors, and in our experience they are best managed in the same manner as carcinomas. There are, however, many advocates of treatment with simple mastectomy with or without irradiation.

### Summary

The clinical characteristics of the commonest breast tumors are very briefly surveyed. The methods used in the Henry Ford Hospital for the management of these lesions, and especially of carcinoma, are outlined. It is stressed that every tumor of the female breast deserves and commands one's most earnest effort for diagnosis, for the diagnosis of all of these tumors must be regarded as the differential diagnosis of carcinoma.

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## Nutrition and Infection

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**S**TUDIES OF INFECTION during the past forty years have concerned themselves largely with the problems of the identification of specific organisms, variations in virulence, modes of transmission, and specific immune response—attention has been focussed on the organism. And yet the soil upon which the seed must be planted would seem to be of at least equal importance with the infecting agent. The experienced clinician has based his prognosis in a given disease as much on the nutritional state of his patient as on the type of organism with which he is infected. Numerous examples of what I have in mind will occur to anyone. The enteric disturbances of infancy which claimed such a heavy toll in the summer months did so only in that group of patients who were already poorly nourished. In a large service devoted almost entirely to the indigent infant under two years, an analysis of the previous histories of those who died in the summer months showed almost invariably that from a nutritional standpoint they had been undermining the resistance to what might have proved a relatively harmless infection, for at least six months before they became ill. Infectious diarrhea may occur in any economic stratum but its course will be determined by the previous nutritional state of the patient. Rheumatic fever and chorea are notoriously diseases conditioned by economic status, which in turn is the chief factor affecting nutrition. A good diet is relatively expensive; a poor one may be very cheap. In an outpatient clinic where I have worked for nearly twenty years, we have seen seventy-five cases of chorea. During that time there have been over a quarter million office visits, a large percentage of them supervisory checks of normal children born in the same institution. There was not a single instance of chorea occurring in the children whose nutritional state had been supervised. In that same institution during that time there were 225 cases of rheumatic fever and rheumatic heart disease admitted to the inpatient service among 15,639 admissions. Of these,

sixty came from the extremely indigent group, orphans committed to the care of a foster home agency. Of the remaining, only seven had been seen previous to the development of the rheumatic state, and only two had been followed from birth. I have seen a moderate amount of rheumatic fever among well-cared-for patients in the office, but it has run a curiously abortive course, and my original poor prognosis on finding the condition has had to be revised an embarrassing number of times. Coburn contributes an interesting study on this point in a study of 100 children in New York City, half from the upper and half from the lower economic stratum. The notable deficiencies in the diets of the poor group were in protein, calcium, vitamins A and D, and iron. The correction of these defects in half the poor group led to a notable reduction in recurrences. Even the supplementing of the diet with eggs in a home for rheumatic children seemed to result in a failure of streptococcus infections to produce exacerbations in the rheumatic state. A similar observation was made at Christ's Hospital, London, when recurrences fell to one-third with an increase in the diet of milk and butter. This was attributed to the added fat, but this would seem gratuitous when those items likewise increased so sharply the intake of protein and calcium.

Cannon's studies along this line, that relate nutrition particularly to the development of an acute infection, stress the role of the serum globulins as the source of immune substances, and he sustains the thesis well that "any condition which affects protein metabolism either by leading to depletion of the protein reserves or by interfering with the adequate intake of high quality proteins may depress resistance (1) through the reduction in the quantity and quality of the phagocytic tissues, or (2) through its adverse effects upon the antibody mechanism."

In the tuberculosis field, the relation between an inadequate diet and increased incidence of the disease is almost taken for granted. Critical studies are difficult of evaluation, since mass dietary deficiencies are usually not separable from other socio-economic factors, such as housing conditions leading to increase in contact, and lessened medical care. Probably the study most often quoted is that of Faber in Denmark at the time of World War I. A 30 per cent rise in the mortality from tuberculosis occurred in 1916-17; a similar rise

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was noted in the belligerent countries and in Holland, which was continued until the end of the war. In Denmark, however, unlike these other countries, there was a prompt fall following a blockade which prevented the export from that country of foodstuffs, chiefly meats, fish, butter and probably milk—again items which were high in protein, calcium, fat and vitamin A. Our own studies are confined to this field and will be presented later.

In attempting to relate nutritional state to the occurrence or course of infection, our first problem is an adequate appraisal of nutrition. The weakness of simple measurements of height and weight is well recognized, though these become more worthwhile in children when the curve of growth over a significantly long period of time can be plotted in some such way as Wetzel suggested. Even so, gain in weight may be deceptively adequate over many months while basic substrates such as nitrogen and calcium are being lost to the body, and conversely, desirable losses in weight may be effected by the obese while nitrogen and calcium are being normally stored. One of the factors unfavorably influencing the storage of calcium and phosphorus, and thus increasing the possibility of rickets, is an increased speed of growth. We have used as our measure of nutritional status the retention of nitrogen and calcium as reflected in balance studies.

To clarify what follows, a few words may be appropriate about the laws governing the retention of nitrogen and calcium. Being basically structural substances, they behave quite differently during the period of growth, the period of maturity and the period of senescence. The growth phase extends roughly through and is apparently limited by the attainment of sexual maturity, and since this varies a great deal, the measurement is physiological rather than chronological.

In the mature individual, increases in the intake of nitrogen do not result in its retention within the body unless there has first been created a deficit which requires filling; the normal picture is one in which intake and outgo are equal. In the growth period, retention quantitatively varies with the several spurts of growth, being extremely high in infancy and in the period just preceding the onset of sexual maturity. In the growth period, increases in intake will be accompanied by increases in retention only up to a certain point, beyond which the excess is rejected. In a general

way, the metabolism of calcium follows that of nitrogen, though there are marked exceptions to this. Both are influenced by the entire endocrine system either directly or indirectly.

In general, the following major factors influencing retention have been studied, and some consideration given to their effect on the tuberculosis process: (1) diet, (2) vitamin D, (3) the endocrines, (4) the phase of growth, (5) infection, and (6) activity and rest.

First, as to the adequacy of the diet itself, we can speak from experience only in the case of children. We have measured this and feel definitely that the protein requirements particularly in the pre-puberty period is higher than commonly used—higher than recently recommended by the National Research Council; it proved in many cases to be 15 per cent of the total calories of an otherwise adequate diet, though 13 per cent did satisfy many, as judged by the nitrogen balance. The calcium requirement at this same period would be approximately 1.4 gm., or the amount represented by a quart of milk, an egg and average intake of vegetables.

Regarding the role of Vitamin D, excellent data are available to show the need for this in the period of infancy and childhood, but little effect was observed when growth had ceased. The further warning should be noted that, like thyroid, moderate doses may be anabolic while large amounts may reverse this. There is evidence that, again like thyroid, increases in the basal metabolism follow its use. The requirement during the period of accelerated pubertal growth would seem to be higher than that in the period of more stable growth. We have recently found in five cases of epiphyseolysis that a failure to store normally could be immediately corrected with an adequate intake of calcium and vitamin D, and that metabolically this condition was like infantile rickets though the blood did not reflect this. Histologically that condition is not like rickets.

Regarding the influence of the hormones, space will permit only a mention of possibilities. The growth-promoting factor of the anterior pituitary will increase storage but as yet has, in our hands, had no practical value since anti-hormone develops rapidly and prevents a continuation of any effect. In children, as opposed to adults, lowered metabolism referable to thyroid carries with it poor retention which can be improved by administering thyroid; but likewise,

abnormally elevated metabolism associated with toxic goiter also diminishes retention. Both of these phases of metabolism may occur as exaggerations of a normal physiological tendency to a pre-puberty rise and post-puberty fall, and should be watched for by the physician caring for the adolescent. In the girl at puberty, we have been able to show a definite depression with the estrogenic hormone, though it is reported that the reverse of this occurs in senescence. All of these findings merely emphasize the fact that there are at play a large number of glandular factors basically influencing nutrition quite independently of dietary intake.

The role of focal infection has been studied, and in the case of chronically infected tonsils a definite fall in basal metabolism, together with a marked improvement in the retention of nitrogen, followed tonsillectomy; in some instances the fore-period showed negative balances on an adequate diet, a fact which brings out graphically the importance of the detection and eradication of foci of infection in the promotion of optimal nutrition.

The story of the metabolic change incidental to sexual maturation when written in terms of metabolism brings out a striking depression of the retention incidental to the onset of menstruation in the girl. Considering growth patterns it might be expected that similar changes would occur in the boy several years later. Finally a comparison of retentions during rest and activity shows a striking fall in the ability to retain these items with bed rest, and that this state is definitely unphysiological, as Dock has so strongly stressed, and any advantages it may have should always be carefully weighed against its repeatedly demonstrated demineralizing effects.

To summarize this phase of the work, we have tried to point out a group of things which affect the storage of nitrogen and calcium, to make clear that this is not simply a question of securing an adequate intake of food but rather involves a consideration of a number of factors which can be brought out only by a thorough medical survey, which includes a good history and a complete physical examination. Dietary surveys fall considerably short of this.

Our studies attempting to relate nutrition as measured by the nitrogen and calcium balance have been made largely on two groups of children, one a group showing the first evidence of reinfection-type lesions, and the other well developed

conditions under treatment. In the course of following regularly, for varying periods up to eighteen years, 1,100 tuberculin reactors removed from contact and placed in foster homes, wards of the Society of St. Vincent de Paul, we have found thirty-six reinfections, few of them advanced. These were hospitalized promptly and studies undertaken. When these healed without complication, the storages of nitrogen and calcium were high, so abnormally high in some instances that it could be understood only as a filling of depots which had been depleted by previous starvation. Several subjects showed a failure of storage for various reasons, and it was characteristic of these that healing did not occur, or even that frank spread of the process was evident. In one instance in which nitrogen was well stored, a reinfection lesion in the first two interspaces regressed slightly, but a fresh lesion appeared surrounding the old calcified Ghon tubercule. In this child, calcium was being lost for four months before this occurred. The commonest causes of an inadequate storage seemed to be (1) an underestimation of the requirement for growth and healing, (2) the metabolic changes incidental to puberty, and (3) intercurrent infection.

It is felt that these studies bring out a relation between nutrition, as measured by the nitrogen and calcium balances, and reinfection tuberculosis and its course.

### Summary

1. In an eighteen-year study of tuberculin reactors removed from contact, endogenous reinfection was demonstrated in about 3 per cent of cases.
2. Balance studies suggested that the factor largely responsible for the development of the reinfection was a nutritional one.
3. The factors influencing an optimal retention of nitrogen and calcium for growth, and at the same time the integrity of the primary lesion, are manifold—dietary, infectious, glandular.
4. The provision of adequate stores for growth of these substances is likewise essential to healing of a lesion already developed.

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## Control of Virus Infections

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THE BASIC CONCEPT of control of infectious diseases, in general, lies in vaccinia-Jennerian prophylaxis as demonstrated in 1798. Here a virus, probably of modified nature, was shown to give rise to immunity against the more severe natural infection. It remains one of the most consistently effective of all vaccines, and because of this the idea has persisted that immunity in virus diseases is best induced by modified disease. In fact, this thesis persists in the general concept of immunization. For a considerable period it was believed that only by the use of active virus could immunity by vaccination be attained.

The notion was further enhanced by the Pasteurian vaccination against rabies. In that instance the virus of rabies was modified by passage through rabbits until it had reached a fixed stability of reduced virulence for the natural hosts and man. Under these circumstances, repeated inoculations of virus, graduating upward in activity, were employed for prevention of disease. The vaccine, owing to the prolonged incubation period of rabies, could be administered after the injury but before the onset of signs of infection. The limitations were that in injuries about the face the effect was less evident. In efforts to control the disease, vaccination of dogs was undertaken. The results were inconclusive, and the immunizing potency of the preparations was poorly established. In recent years, however, with increasing virus content of vaccines, even inactivated materials have with single injections in dogs proved to be effective in eliminating rabies in canine populations of several states.

Control of yellow fever had centered in the concept of eradication of the disease by elimination of the known vector, *Aedes aegypti*. In certain areas it was apparently accomplished. With the recognition of jungle yellow fever, a disease epidemiologically distinct from the clinical disease, in that it was not urban but jungle in nature, the problem enlarged. It was shown that monkeys and marsupials apparently could serve as the reservoir, and that species of mosquitoes living in tree

tops served to transmit the disease. In the cultivation of virus in tissue culture, a spontaneous mutation was encountered, yielding a strain 17D. This strain no longer produced the characteristic disease in human individuals or in experimental animals. In the human, little or no evidence of disease was encountered, but the virus circulated in the blood and produced staunch immunity. This attenuated virus has been shown to be remarkably effective in the prevention of the natural disease.

The examples given all represent immunity induced by modified strains of active virus which produce subclinical disease and persistent immunity. The pattern has been followed in recent studies of immunization against distemper and cattle plague.

For a considerable time the concept was maintained that only by modified infection (active virus) could immunity be reduced. Early in the studies of influenza it was demonstrated that inactive virus could induce resistance to the active agent. Moreover, when given by routes other than respiratory, immunity was created. The studies which followed have demonstrated that virus cultivated in the embryonated egg can be inactivated by mild treatment while retaining the capacity to stimulate antibody production and immunity. In the extensive studies against influenza A, a distinct effect was obtained, and against influenza B the results were even more distinct. That the effect is not a permanent one is not surprising since the disease itself gives but a transient immunity. But the evidence points to a persistence of enhanced resistance for months; at least, probably extended to last over a respiratory season. It should be emphasized that this represents a clear demonstration of resistance induced by inactivated, non-infectious virus.

In animals, the equine encephalomyelitis virus and probably the Japanese B encephalitis virus appear also to be combated by the use of inactive virus vaccines.

Control of virus diseases has been largely limited to the application of prophylactic active immunization, because by the time the clinical symptoms of disease appear, the essential cellular injury has taken place. In recent years, however, two examples of prophylactic passive immunization against virus diseases have become clearly demonstrated.

Presented at the first annual Michigan Postgraduate Clinical Institute, Detroit, March 12, 1947.

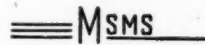


In measles the use of convalescent serum or of purified gamma globulin which contains the specific antibodies is well established. The point of interest in this passive immunological prophylaxis is that the effectiveness diminishes as one progresses from the time of exposure toward the onset of clinical disease. This deterioration in effect appears to parallel the development of the virus infection. If given early, even though the virus may have entered protective cells, the serum can prevent its transference to other cells and prevent the development of a sufficient bulk of infection to establish the disease; later, as the agent has become more diffusely entrenched in cells, the serum can serve only to modify or still later have no effect. The alteration in effect of immune serum seems to mark stages in the development of the virus disease.

In the past few years, Stokes and his associates have shown that infectious hepatitis (catarrhal jaundice) can also be prevented by the use of gamma globulin in the incubation period of the disease. When given in amounts of 0.08 to .15 c.c. per pound, it has been shown to prevent the disease if given six days or more before onset. Here, again, the preventive effect can be of great value in epidemics involving institutions or other closely associated groups. The effect seems clearly to indicate that the period of blood-stream invasion is an important stage in the pathogenesis of infectious hepatitis. The effect in serum jaundice with the prolonged incubation period has been less evident, but there are suggestions that repeated injections of antibody may have an effect here as well.

Therapeutic control of virus diseases has been of little significance except as it counters the secondary infections so common in measles, influenza, smallpox and others. There is one group of agents usually classified among the viruses in which, however, sulfonamides and antibiotics have shown consistent beneficial effects, experimentally and clinically. This is the psittacosis-lymphogranuloma group of viruses, characterized by elementary bodies, by carrier infection and by relapses. They are now classified as of the family Chlamydozoon. They are intracellular as are the other viruses but they have been shown to be susceptible to sulfonamides and penicillin. Psittacosis and ornithosis patients treated early and consistently with 200,000 or more units daily for several days after the fall of fever have been shown to respond well. Lym-

phogranuloma venereum has been less thoroughly documented but is also favorably influenced. The effect with these viruses indicates the probability that a therapeutic approach to virus infection is not as hopeless as has been commonly suggested. The response of agents such as those of tularemia, brucellosis, tuberculosis and other intracellularly disposed organisms may furnish a pattern for further advances upon the microbial midgets—the viruses.



## TUMORS OF THE FEMALE BREAST

(Continued from Page 562)

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## Prevention of Tropical Diseases

By Hardy A. Kemp, M.D., Dean  
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EARLY CONCERN as to the possible spread of tropical diseases in America, and in the northern states especially, following the return of troops from tropical areas, now appears to be groundless in spite of a considerable number of recurrences of clinical malaria in veterans who contracted the disease during their war service. It appears that no secondary cases have developed, nor does it appear that there is any real cause to think that malaria will again be established in the northern states. Species of anopheline vectors present in this area are few in number, and those prevalent are not regarded as dangerous in their transmitting potentialities. It would further appear that there is no danger at all as to the establishment and spread of more strictly tropical diseases such as filariasis, kala-azar (visceral leishmaniasis), schistosomiasis or other diseases known to be of trematodal origin. Intestinal parasitism, although something of a factor in our troops serving in tropical campaigns, is scarcely to be considered at all, except in individuals who are still carrying large numbers of their parasites. Again, such instances indeed are quite rare.

The dysenteries, both bacillary and amebic, while generally considered as tropical problems, are nevertheless to be regarded as health factors throughout the world. In both instances, the carrier state very often becomes firmly established and may become a source of epidemic disease. Both bacillary and amebic dysentery have long been known to occur in temperate and even arctic parts of the world, but are too frequently missed in diagnoses because they are too often regarded as tropical or semi-tropical in their occurrence. It is indeed possible that some of the outbreaks of dysentery, whatever the exciting cause, might arise,

or might have arisen, from returned veterans of tropical service.

The almost incredibly rapid forms of air transportation to and from tropical parts of the world necessarily are accompanied by a certain amount of danger as far as occurrence and spread of tropical disease is concerned. Fortunately the spread in Michigan is likely to be limited by the absence or near absence of the specific vector and by the high standards of American sanitation.

As far as travel in the tropics is concerned for business or for recreational purposes, it might be pointed out that the two commonest disease processes, malaria and the dysenteries, are preventable, first, by attention to mechanical protection from mosquitoes in the case of malaria, and, in the dysenteries, by the use of caution, as far as possible, in selecting articles of food and in the use of drinking water. Green vegetables in an uncooked state are still to be considered potentially dangerous in tropical parts of the world where the raising and handling of these articles is still on a primitive scale. Water supplies in tropical parts of the world are, for the most part, still unsafe. American methods of water purification are yet to be installed. The boiling of water for beverage purposes, although an unhandy procedure, is still the safest and best, and is to be preferred over any amount of treatment methods applied on a small scale.

Preventive vaccines, including typhoid, are in themselves no absolute guarantee of safety if one expects to visit tropical parts of the world, where certain diseases for which we have a vaccine are likely to reach epidemic proportions.

Much is made particularly of Asiatic cholera and the terrifying proportions it very often reaches in the Orient. India, China and Polynesia are constantly scourged by this disease, and while few cases ever occurred in American personnel, it is likely that its prevention was due to American sanitation and American cleanliness, rather than to American or British vaccine. To this might very well be added the resistance of the healthy American as compared to the undernourished and chronically diseased Oriental.

Typhus vaccine has proved highly effective against louse-borne typhus, although it is to be recalled that louse-borne typhus is not particularly a disease of the tropical parts of the world, but is more common to the temperate zones. However,

Presented at the first annual Michigan Postgraduate Clinical Institute, Detroit, March 12, 1947.

in winter months the semitropical parts of the world have very often had large epidemics. At the same time, it appears that the same vaccine is effective also against flea-borne typhus, which is common in endemic form throughout the tropics. No vaccine, however, was developed during the war for so-called scrub typhus, which, before the end of hostilities, came to be regarded as Tropical Disease Enemy No. 2, and second only to malaria. Fortunately, scrub typhus is not a factor within cities and towns, but is only encountered in brush and jungle portions of the tropical world.

Whereas, yellow fever has practically disappeared and is said to exist only in the hinterlands of Africa and Brazil in the so-called jungle form, nevertheless, it is to be regarded as a great danger which, although quiescent at the time, might very well reach epidemic proportions, and without warning. The mosquito vector of yellow fever is present in very large numbers throughout the tropics where American methods of mosquito control are not employed. Unfortunately, other governments have neither the money, nor the energy to enforce such precautions as ours. In this connection, it is interesting to note that travelers to India, who, in the course of their journey expect to touch at Brazil and the central portions of Africa where yellow fever is still regarded as being endemic, are not allowed to land in India until the incubation period has elapsed since departure from the African or South American continent. The same is true for those who have been vaccinated against yellow fever, since the vaccine itself is a live virus, and, therefore, carries the threat of introducing the disease in mild form in a highly susceptible population where the mosquito vector occurs in an uncontrolled abundance. Needless to say, air travel to India through non-yellow fever parts of the world, namely, the temperate zones, does not require yellow fever vaccination prior to the trip, and if the traveler does not touch the yellow fever portions of Africa, the government of India will allow entrance without question in this regard. India has been successful over these many years in keeping yellow fever out of that vast reservoir of highly susceptible individuals, and the government of India means to prevent, if humanly possible, such a holocaust as would occur if yellow fever were ever introduced there.

Dengue fever and sandfly fever, both highly

prevalent in the tropics, are preventable by protection from insect vectors of these two diseases and in no other way. Unfortunately, one has difficulty in going about his daily tasks or recreation encased in a costume suitable to withstand the assaults of *Aedes aegypti*, a daytime biter, and the nights are even more uncomfortable if one must try to sleep beneath a netting thick enough to keep out the various species of genus *Phlebotomus* which might be present. Fortunately, neither of the two diseases is fatal, although very often convalescence is long and uncomfortable.

One would do very well indeed to renew one's protection against smallpox well in advance of a sojourn into the tropics where this disease still occurs in a most vicious form. Indeed, there have been instances wherein vaccinia has failed wholly to protect against variola in tropical epidemics.

For the most part, inoculations for all the diseases preventable by inoculation in one form or another are either handled, or insisted upon, by immigration authorities and other officials connected with the handling of visas. These inoculations, however, must not be regarded as affording complete protection in any sense of the word against the prevention of disease, and the individual himself, or his physician, should certainly see that everything possible in ways other than vaccination is done in the way of protection.

One of the bacterial infections, or one that might indeed be complicated by virus, has not yet been mentioned, although it very often accounts for many tragic events in what was undertaken as a holiday. I refer to pneumonia. In the tropics, pneumonia strikes without warning, and very often for little reason as far as the individual is able to ascertain or understand. Not uncommonly the tropic sojourner overindulges himself in many ways, and is likely to suffer exhaustion and what really amounts to exposure when he least expects it. The result too frequently is a pneumonitis which in no way follows the classical pattern, nor yields too readily to the forms of therapy ordinarily successful in temperate parts of the world. Too little is known about pneumonia in the tropics. It seems likely that it is both a virus and a bacterial infection combined. In any event, it is very likely to be fatal within a matter of days after onset, and is to be highly regarded as a potential danger in any instance of its occurrence in the tropics.



# Editorial

## RUGGED INDIVIDUALS

AMERICA IS A GREAT country, one in which we take pride, and one where we would rather live than any other on this green earth. Such a trite statement! In all seriousness, what did make the United States a great and worthwhile home for a rugged and manly race of men?

Our fathers came to America in order to find freedom from restraint, in order to find a place where they could work as they chose, and could make as great a future for themselves as they were capable. Individual effort—individuals striving for more and greater opportunities—individuals doing the things that would make their lives and those of their families more abundant, more fruitful, and more expressive of content and well being.

Homes were made in the wilderness with the help of a few friends, or alone, depending upon one's own strong arms and determination to get ahead. Communities grew and thrived, and in the end came independence which was not given but was hard earned. There were such leaders as George Washington, Benjamin Franklin, Thomas Jefferson, Benjamin Rush, Alexander Hamilton, Abraham Lincoln. And during those formative years, men were ready to assume their responsibilities and to make their opportunities.

But years have rolled by, and we find that people are more interested in security. Security is much more important than opportunity. The ambition is so to plan that the future will take care of itself. There will be no worries. We shall be able to stop at some undefined place in our progress, sit back and have everything handed to us from that time henceforth. That may not be the exact line of thought, but that is the logical conclusion.

Senator Wagner, he of the Social legislation in Washington, has complained that the new Taft-Ball-Smith-Donnell Bill, S.545, does not provide free health care for the multitudes, but requires a means test for free care. Senators Taft, et al, on the contrary, have seen the vision of a great and free people who, if allowed and given an opportunity, will make their own way. These gentlemen have given us a measure whereby any individual who wishes may make his health services

secure, because there will be non-profit or other plans working, and he can use them, if he wishes.

If the American people through Congress will avoid the sugar-coated "life of Riley" so glowingly displayed by propanganda of every sort and from the very fountain heads of government planners—if they will look into the past and ask what made us what we have been these many decades, they will surely follow the lead of men of the same calibre as those out of the past. Vision in planning our future health and welfare is just as important now as it was in the days when we were making the world's first great Republic.

That vision is still with us—there are still clear-thinking men who look to more progress, greater opportunities, and a more abundant life. Beware of false prophets. Wagner—Murray—Dingell—Falk—Altmeyer—Parran have all tried to force a philosophy upon our people which carries too much soothing syrup.

What we need is ambition, resolution, energy, valor, an unconquerable spirit, and the will to make our future for ourselves; not to have it rubber-stamped for us.

## MICHIGAN POSTGRADUATE CLINICAL INSTITUTE

THE FIRST ANNUAL Michigan Postgraduate Clinical Institute was held at the Book-Cadillac Hotel in Detroit on Wednesday, Thursday and Friday, March 12, 13, 14, 1947, under the sponsorship of the Michigan State Medical Society, with the co-operation of the Wayne County Medical Society, the University of Michigan Medical School, the Wayne University College of Medicine, the University of Michigan Department of Postgraduate Medicine and the Michigan Foundation for Medical and Health Education, Inc.

This institute brought together for the first time six great organizations in the field of medical education and research, and in the most active form of a clinical postgraduate institute for the practitioners of medicine of Michigan and the surrounding states of Ohio, Indiana, Illinois, Wisconsin and Ontario. The total registration was 1,293. Of these, 1,082 were doctors of

## EDITORIAL

medicine with 113 registered from states other than Michigan.

Three days of conferences, symposia and panel discussions were enjoyed. The entire program was given by our own Michigan men, many of them the younger and more active leaders. We have demonstrated that Michigan can lead in medical thought as well as in economic and sociological advance. The young teachers, brought to this conference, have set a goal that will be difficult to surpass in another year, but one that is a challenge which we shall attempt to meet.

Most of the talks and discussions were made from notes or slides, and were not presented as formal papers. Abstracts of most of them, as well as several of the complete papers, will be published in about two numbers of *THE JOURNAL*. The articles are grouped in this way in order to emphasize the importance of this institute, and to stimulate a repetition next year.

We are proud of this demonstration of ability, and of the men partaking.

### THE SPASTIC CHILD

SEVERAL CLINICS held lately in Michigan regarding the spastic child, have called this unfortunate problem to the attention of parents and doctors who must care for and treat the condition. Until recently these children were cared for as they arrived, and in the only way possible, physicians doing what they could with the knowledge and facilities at hand. The cause of the disease was only partially guessed at, and the treatment mostly inadequate. Many children were institutionalized and seen as little as possible by their parents and relatives.

Many of these children were considered morons; others supposedly not bright; some never became able to care for their daily needs and necessities, and others never could walk or dress themselves. In addition to the physical handicaps of the spastic child, those who have had experience with a large number report that they have a greater degree of emotional vulnerability than from any other physical handicap. They are especially prone to sensitivity and easily hurt in their feelings. The spastic child becomes a severe problem to all concerned. Many of these children have normal or above normal intelligence. Some surprisingly become active and useful citizens.

But now they have come into their own, so to

speak. We now know much of the problem and care, and we have some doctors who have made sufficient study to give good advice leading to the making of useful citizens. The numbers of these cases are appalling when reduced to figures, and present an argument for more study and more needed provision for advanced and suitable care.

Seven spastic births every year out of a hundred thousand persons is a number to demand attention. One of these children will not survive, but six children with birth palsies each year out of a community of a hundred thousand people is a figure just as impressive as the approximately equal appearance of poliomyelitis. These children, as a rule, are born with their affliction, instead of attaining a degree of growth before being stricken. That fact minimizes the shock, and has so far militated against demand for research and study, it being accepted that nothing could be done.

Modern study and knowledge, however, prove that much can be done to ward off the disease, and to help these children overcome their handicap. Some of them are going through school and college, some are graduating into the professions. Typewriters and other aids have worked wonders.

We have drives and studies for the care of poliomyelitis, cancer, tuberculosis, rheumatism, the crippled child. Will the next great movement be to solve the problem of spastic paralysis?

The Michigan Society for Crippled Children and its leaders are working along this line with much enthusiasm and hope of success.

### ON THE RUN . . . . .

Because dicoumarol lowers the prothrombin level of the fetus it should not be given to pregnant women.

\* \* \*

Calcium penicillin in wax and oil is responsible for allergic reactions in 5 per cent of patients in whom it is used.

\* \* \*

Chances are 10 to 1 for recovery in myocardial infarction but 10 to 1 against recovery in dissecting aortic aneurysm.

\* \* \*

Engorgement of neck veins with increased venous pressure may be due to congestive heart failure, cardiac tamponade or pulmonary embolism.

\* \* \*

Acute pancreatitis may respond favorably to paravertebral block.

Selected by W. S. REVENO, M.D.

# Detroit Physiological Society

Session of March 20, 1947

## The Pharmacology of a Series of Compounds Structurally Related to Hydroxytyramine: An Analysis of Vasodepressor Action

A. M. Lands, Frederick Stearns and Co., Division of Sterling Drug, Inc., Detroit 31, Michigan.

The intravenous injection of epinephrine may cause a rise, a fall or a rise followed by a fall in blood pressure, depending upon the amount of drug injected. In order to better understand this dual action, a series of compounds structurally related to hydroxytyramine have been studied for their effect on blood pressure. The most effective vasoconstrictor is d,l-norepinephrine, being 1.3 more potent than d,l-epinephrine. The replacement of the N-methyl group of epinephrine by larger alkyl groups leads to a loss of pressor action. The depressor effects which may be elicitable with epinephrine are prominent when the N-alkyl group is -ethyl, -isopropyl, -sec.-butyl or -tert.-butyl. It is weak when the N-alkyl group is -n.propyl or -n.-butyl. Greatest vasodepressor action was obtained with the N-isopropyl homologue (Isuprel).

If the alcoholic hydroxyl is removed from the beta carbon of Isuprel, depressor action is greatly diminished; if converted to the corresponding ketone, depressor action is abolished. The removal of one or both hydroxyl groups from the benzene ring of Isuprel diminishes depressor potency. The structural requirements for vasodepressor action appear to be as specific as those required for vasoconstrictor action.

Bronchodilator action was determined by lung perfusion and in unanesthetized guinea pigs exposed to histamine mist. Effectiveness as a bronchodilator corresponded to the effectiveness of the compound as a vasodepressor agent. Thus, norepinephrine is a poor bronchodilator and a good vasoconstrictor; Isuprel a good bronchodilator and a poor vasoconstrictor. Epinephrine is a more effective bronchodilator than norepinephrine but is less effective than Isuprel.

Comparable results were obtained on other smooth muscle organs relaxed by epinephrine. Thus, Isuprel will relax the isolated guinea pig

ileum in a dilution of 1 part in 50 million, and the isolated rabbit uterus 1 part in 20 million. Similarly, these organs *in situ* are relaxed by Isuprel in intravenous doses of 0.1 to 0.5 mgm./kgm.

The N-alkyl homologues of epinephrine have comparatively low toxicity. In albino mice, epinephrine has an L.D. 50 to 4 mgm./kgm. by intraperitoneal injection whereas Isuprel has an L.D. 50 of 450 mgm./kgm.

## A Substance Derived from Bovine Plasma Which Produces Leukopenia and Lowers Blood Pressure

M. Mason Guest, Robert C. Murphy, Arnold G. Ware, Stephen R. Bodnar and Walter H. Seegers, Department of Physiology, Wayne University, College of Medicine, Detroit, Michigan.

A protein, relatively heat stable to 90°C, has been derived from the euglobulin fraction of bovine plasma. When injected intravenously this substance produces a lowering of the blood pressure in the dog and guinea pig which approximates 40 to 70 per cent of the initial pressure. Recovery usually occurs within ten to fifteen minutes, but a secondary fall frequently ensues. If sufficient material is given an irreversible shock-like condition results.

Following the intravenous administration of the bovine plasma fraction the leukocyte count in the blood from the femoral artery and vein falls within two to three minutes to an average of 1/15 of the initial value. The decrease in white cells does not appear to be correlated with the fall in blood pressure. The differential pattern is usually reversed so that for a period of time the lymphocytes become much more numerous than segmented forms. Sedimentation rates and hematocrit values are not affected significantly.

In perfusion experiments this protein material causes the isolated turtle heart to stop in diastole, or if visible contractions continue, the cardiac output falls to or near to zero. Recovery occurs within two to three minutes if the substance is ejected from the heart cavities.

The tonus of smooth muscle of the rabbit in-

(Continued on Page 606)



# TWO

## DISTINCTIVE PENICILLIN PRODUCTS

### 1

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# Michigan's Department of Health

WM. DE KLEINE, M.D., Commissioner, Lansing, Michigan

## MICHIGAN CANCER DEATHS INCREASE

Cancer deaths in Michigan increased 4 per cent in 1946 and have increased 17 per cent since 1940, according to provisional figures. There is an increase in cancer deaths among infants and children under ten, and an increase among people over forty. Almost 200 more males in Michigan died of cancer in 1946 than females. There is a decreasing trend in cancer deaths among females and an increasing trend among males. A contributing factor in the uptrend among males is lung cancer between twenty and forty-five years of age. Cancer, second cause of death, took 7,751 lives in Michigan in 1946, provisional figures indicate. One person in seven dying in the state, died of cancer; the national average is one in eight.

## NEW HEAD AT RAPID TREATMENT CENTER

Fred O. Henker, II, M.D., arrived in Ann Arbor, April 5, to become medical officer in charge of the Michigan Rapid Treatment Center. Dr. Henker is a graduate of the University of Arkansas School of Medicine. He entered the United States Public Health Service and served at Marine Hospital, Baltimore, and at West Tennessee Medical Center, Memphis, where he did venereal disease work before coming to Michigan. He succeeds C. A. Smith, M.D., who has accepted a position with the University of Michigan Hospital.

## RABIES ALARM IN SOUTH STATE

The incidence of rabies in Michigan has been increasing by more than one case a day for the past several weeks. A total of eighty-one cases have been reported to date this year. Five counties, Berrien, Kalamazoo, Van Buren, Cass and Monroe have established dog quarantines. The concentration of new cases in April are in Berrien, Kalamazoo and Van Buren, with a first case appearing in Jackson county. The county incidence of rabies this year follows: Berrien, 29; Kalamazoo, 14; Van Buren, 12; Wayne, 9; Cass, 8; Monroe, 3, and Jackson, Allegan, Genesee, Muskegon, St. Joseph and Shiawassee, 1 each.

## X-RAY STATE EMPLOYEES

A total of 1,812 employees and officials of the state of Michigan were given chest x-rays by a mobile unit of the Michigan Department of Health in March. The unit was set up in the Capitol and in the state office buildings.

## URGE WHOOPING COUGH VACCINATION

The Michigan Department of Health, through daily and weekly papers and via radio, is urging vaccination of all children for whooping cough. A total of 2,882 cases was reported by April 4 in comparison with a seven-year median of 1,710 cases. Between 150 and 300 new cases are being reported each week.

## NEW AID TO TUBERCULOSIS

The Michigan Department of Health has added a new medical social consultant in the Bureau of Tuberculosis Control to assist in co-ordinating the efforts of the Department and other state agencies into a concerted program of assistance to the patient and his family from diagnosis to full rehabilitation. Mrs. Jean Hansen, formerly rehabilitation director of the Ingham County Sanatorium and the Michigan Tuberculosis Association, has been appointed to the consultant's position.

## NEW POLIO CASES

One case of poliomyelitis was reported in Wayne County during the week ending April 4; two cases, one in Wayne and one in St. Joseph County, were reported the week ending March 28.

## VISITOR FROM INDIA

B. S. Yajnik, N.D., Director of the Provincial Hygiene Institute of Lucknow, India, on travel grant from the International Health Division of the Rockefeller Foundation, spent April at the Michigan Department of Health, studying its organization and techniques. Dr. Yajnik's fellowship study of laboratory production and diagnostic procedures in this country is aimed at improvement of the work of his laboratory in India. He requested his study at the Michigan Department of Health.

## EVALUATE HEALTH SERVICES

The fifty-eight local health departments of the state have completed evaluation of their services to their respective communities. The summaries are now being submitted to the Michigan Department of Health and the field staff of the American Public Health Association for evaluation. Consultants of the health department are available to assist the local departments in improving their services and planning their immediate and long-range programs.

## ADVISE IODIZED SALT

Through press and radio, the Michigan Department of Health is again urging the use of only iodized salt for cooking and eating purposes for the control of endemic goiter.

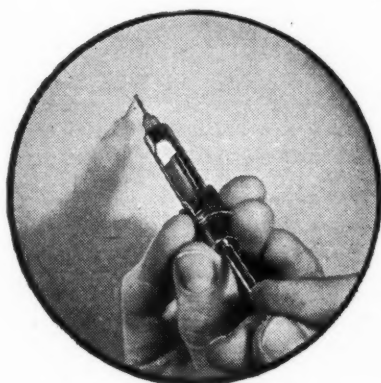
## JOINS TB STAFF

J. R. Brown, M.D., joined the staff of the Bureau of Tuberculosis Control in March 17, on loan from the United States Public Health Service. Dr. Brown, a graduate of the University of Cincinnati, served his internship at Jewish Hospital, Cincinnati, before entering the Navy. He was stationed at an east coast tumor center and later loaned to the United States Public Health Service.

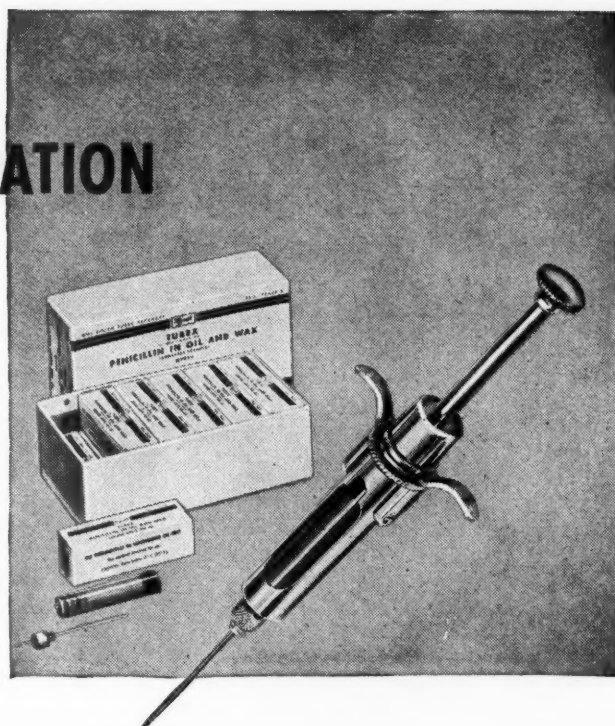
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*Before injecting aspirate to insure  
that needle is not in a blood vessel.*



- Designed for immediate injection — no transfer from ampul to syringe.
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- Tubex has a special safety feature—by aspirating, it is easy to make certain that a blood vessel has not been entered.
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Prolonged therapeutic blood levels (12 to 24 hours) have frequently been observed after a single injection of 300,000 units. Nearly all cases of acute gonorrhea are cleared up by a single injection. Other susceptible coccal infections respond to one or two injections per day.

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Tubex syringes and needles, developed and produced by J. Bishop & Co., are used exclusively by Wyeth Incorporated.



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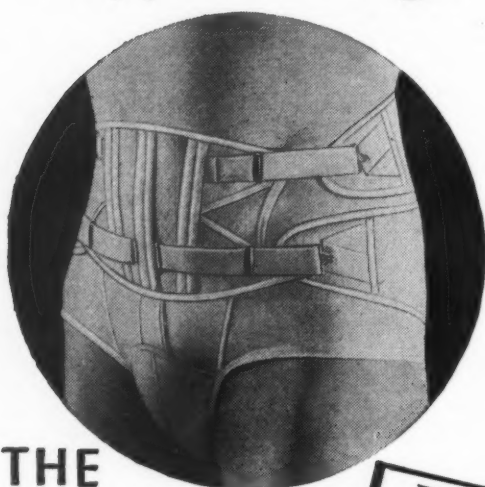
MAY, 1947

*Say you saw it in the Journal of the Michigan State Medical Society*

579



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A. M. A.  
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## Communications

L. Fernald Foster, M.D.  
Secretary, MSMS  
Lansing, Michigan

Dear Doctor Foster:

Permit me to thank you for the beautifully executed diploma of my emeritus membership in the Michigan State Medical Society, signed by you, the President and the Speaker. It is greatly appreciated.

The Society has progressed greatly in recent years. May it continue to prosper. Vivat, floreat, crescat.

Sincerely yours,

EMIL AMBERG.

February 13, 1947

Editor, Journal, MSMS

Dear Doctor Haughey:

Thank you for including my letter on tonsillectomy and poliomyelitis *in toto*. I also appreciate your editorial comments, and the data presented would seem to indicate that tonsillectomy should not be done at all; but I would rather think that at this stage it was a challenge to be more cautious in wholesale removal. I believe that tonsillectomy is indicated where necessary but not just for prophylactic purposes, and that I should have stressed in the letter which you published.

Sincerely yours,  
FRANKLIN H. TOP, M.D.  
Medical Director  
Herman Kiefer Hospital

Wilfrid Haughey, M.D.  
Editor, Journal MSMS

Dear Doctor Haughey:

I enclose a case history which to me seems interesting. It took me eighteen days to "come to" as to the cause of this baby's cyanosis. The case is timely in that the matter was dealt with in the November number of the *Journal of Pediatrics*. As a matter of fact, had I not seen these articles I most certainly would have missed the boat. Are there others?

Sincerely yours,  
ROCKWELL M. KEMPTON, F.A.C.P., F.A.A.P.

### Case History

#### Cyanosis of Twenty Days' Duration in an Infant Under One Month of Age, Responding to Methylene Blue Intravenously.

Baby M. S., aged two weeks, was brought to office, November 4, 1946, because the mother noted baby had been getting blue the past two days. Aside from cyanosis, examination was entirely negative. Weight 6 pounds 11 ounces. On formula of Pet milk, sterile water and Karo syrup.

A visit to the home November 5 revealed a two-

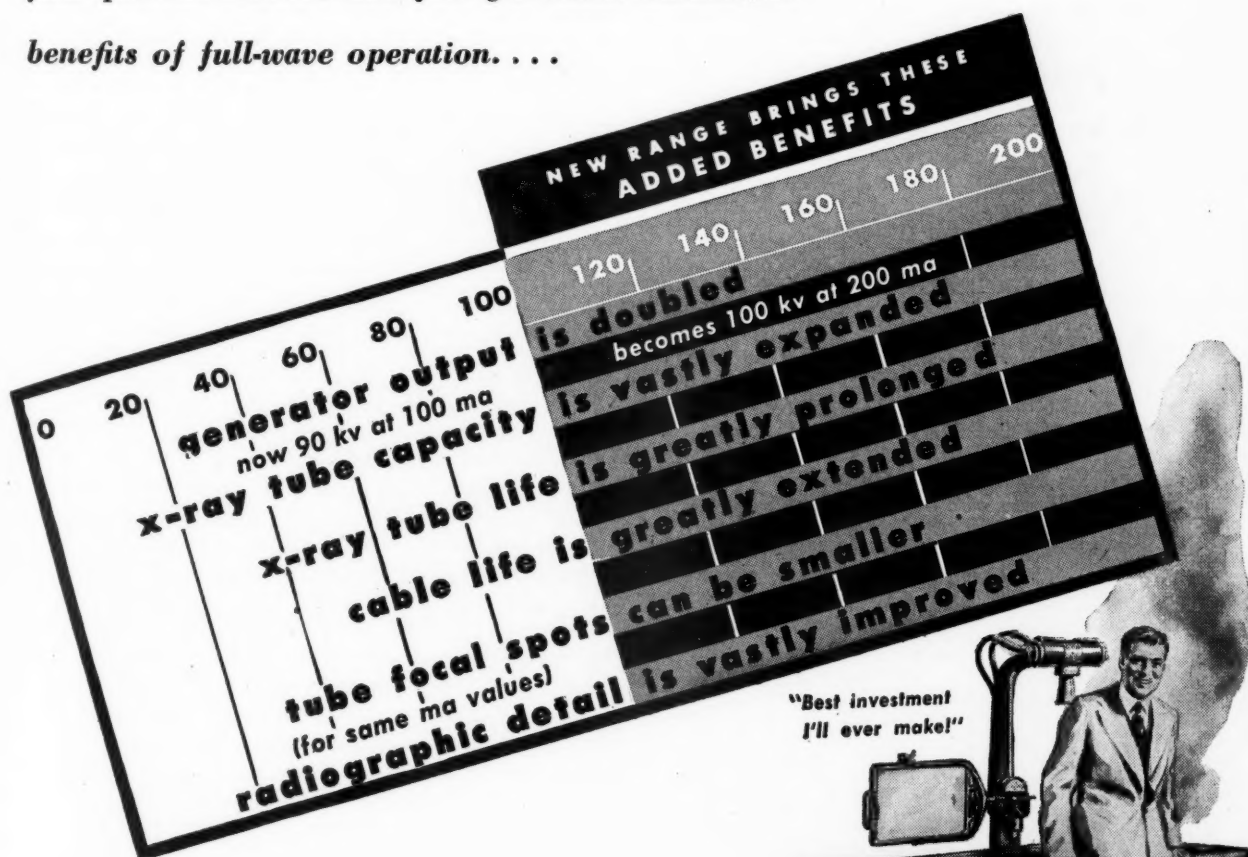
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MAY, 1947

Say you saw it in the Journal of the Michigan State Medical Society

583

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(Continued from Page 580)

room apartment heated by a kerosene stove with no outside vent. The mother was advised to change the environment. The baby was moved to a furnace-heated apartment in the same house. The formula was unchanged.

No improvement in color a week later (November 13). The baby was very dusky and became markedly cyanotic when he cried. He also seemed to be in great distress with his bowels. Cramps were so severe that baby screamed with pain and it seemed impossible to give him relief. There was no vomiting and no diarrhea. Considerable distention was noted but enemas did not help. The parents felt there must be some bowel obstruction. Rectal sphincter seemed rather tight—dilated with little finger and glove. The formula was changed to Similac 1:2 made up in sterile water.

On November 21, on an emergency call to the home, the baby was found to be almost black and appeared dead. He was gathered up in blankets, rushed to the hospital, and placed in an oxygen tent, 50 per cent concentration. After five and one-half hours in oxygen, there was no improvement.

Twenty-four hours later (November 22, 9 a.m.) the baby seemed slightly more comfortable but was still deeply cyanosed. An injection of 0.6 c.c. 1 per cent methylene blue (aqueous) was made in the scalp vein. Within half an hour the cyanosis was almost entirely cleared and the baby was removed from the oxygen tent. At 8 p.m., eleven hours since the injection of methylene blue, the color remained good.

Color was still good November 26. Blood transfusion was given to correct mild anemia. The parents were instructed to use distilled water for the baby.

On March 17, 1947, the baby, now three and one-half months of age, was in excellent condition.

The probable cause of cyanosis was methemoglobinemia resulting from use of high nitrate-content-water in making up the baby's formula. In the rear of the house were two outside privies about seventy-five feet from the surface well pump.

**Conclusions.**—Shallow wells may contain nitrogenous waste. Sterilization of such water may kill all bacteria, but the nitrogen content remains unchanged and, in the presence of a certain bacterial flora in the infant's digestive tract, methemoglobin may be produced. Failure to produce symptoms and signs in the adult members of the family is to be explained on basis of the baby's fluid intake being relatively so much greater than that of the adult. An infant of a few weeks may be taking more than a quart of fluid daily, and many adults take little more than this. Note that when formula was changed to a dry milk the baby was getting 100 per cent contaminated water. It is interesting to note that as the cyanosis cleared, the abdominal distention and pain were relieved, suggesting that these symptoms were on the basis of anoxia.

As a practical point, if the water used in proportion of the formula is in question, it would be well to use a fresh cow's milk formula requiring only small additions of water.

**Note**—This case report was based on clinical observations unsupported by chemical tests on blood or nitrate content of water. For an excellent paper and complete bibliography dealing with subject, see J. Pediat., Nov., 1946.





## Homewood Sanitarium

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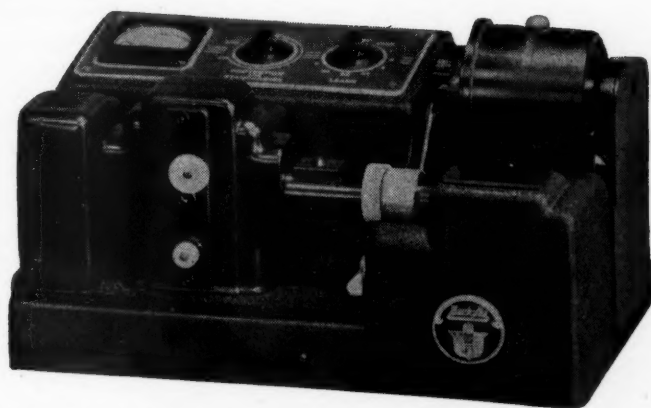
F. H. C. Baugh, M.D., Medical Supt.  
The Homewood Sanitarium of Guelph, Ontario, Limited

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Distinctive and dignified in appearance . . . the Model "E" achieves a new conception in compactness and portability.



This new instrument further distinguished by its moderate cost makes it the pre-eminent electrocardiograph of choice. Call or write us for a demonstration.

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# What's What

You are invited and expected to attend  
the MSMS Annual Session

Grand Rapids, September 23-26, 1947

\* \* \* \* An All Star Cast \* \* \* \*

It will pay you big dividends to attend

The American Medical Association uses each month  
310 tons of paper in its publications.

\* \* \*

According to Dr. Guillermo Diaz of Lima, Peru,  
there is but one doctor to 50,000 persons in Peru.

\* \* \*

Fifty-six hundred veterans with certain disabilities re-  
ceived automotive conveyances at Government expense  
by the end of 1946.

\* \* \*

The Third American Congress on Obstetrics and  
Gynecology will be held in St. Louis, September 8-12,  
1947. For detailed information and the program,  
write 24 W. Ohio Street, Chicago 10, Illinois.

J. H. Ahronheim, M.D., Jackson, is the author of  
"Emotional Albuminuria in Combat" which was pub-  
lished in Psychosomatic Medicine, issue of January-  
February, 1947.

\* \* \*

A nutritional survey is being conducted in Ottawa  
County under the auspices of the Ottawa County Health  
Department and the Nutritional Unit of the USPHS.  
The survey began April 2.

\* \* \*

Renew your federal narcotic license on or before  
July 1, 1947. Send application blank and check to the  
Federal Narcotic Agent, Federal Bldg., Detroit, Michi-  
gan.

\* \* \*

A commemorative stamp has been issued by the U. S.  
Post Office Department as part of the celebration of the  
100th Anniversary of the founding of the American  
Medical Association. The three-cent stamp goes on  
sale June 9.

\* \* \*

Governor Sigler has signed into law a bill requiring  
legislative review of all departmental rules. Under the  
plan any rule can be nullified by concurrent resolution and

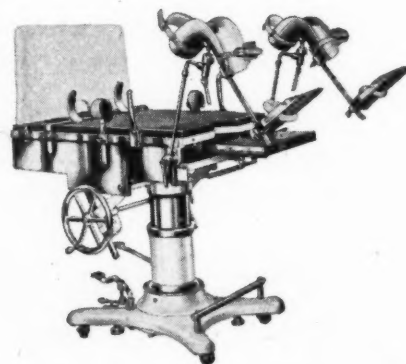
(Continued on Page 588)

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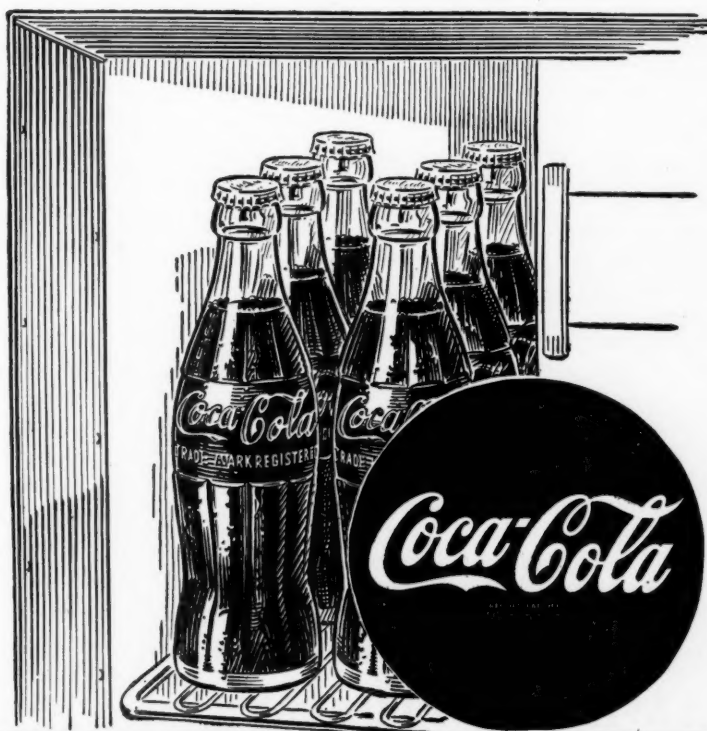
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## The Diagnostic Family is Growing

A new member has been added to the ever-growing Ames Diagnostic Family. The name of the latest arrival is—Hematest.

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(Continued from Page 586)

a joint legislative committee will meet between sessions to approve or suspend rules until the next regular session.

\* \* \*

The National Gastroenterological Association will hold its 12th Annual Convention at the Chelsea Hotel in Atlantic City, N. J. on June 4-5-6, 1947. Program and further details may be obtained by writing the Association at 1819 Broadway, New York 23, N. Y.

\* \* \*

J. W. Logie, M.D., Grand Rapids, has been appointed Chairman, and John M. Wellman, M.D., Lansing, is a member of the Committee on Scientific Exhibits for the 82nd Annual Session of the Michigan State Medical Society scheduled for Grand Rapids next September.

\* \* \*

Henry R. Carstens, M.D.—Announcement of the marriage March 7, 1947 of Doctor Carstens, our former President, and Colonel in Command of General Hospital 17 in World War II, is received. The bride is Miss Coral Bremer of Philadelphia.

\* \* \*

Doctor Wanted.—A. H. Catlin, Village President of Webberville, Michigan, a community of about 700 persons with a "good surrounding territory," writes that his village needs a doctor. There is no one nearer than six miles, and he is too busy to make calls at Webberville.

\* \* \*

A. S. Brunk, M.D., Detroit, Past President of the Michigan State Medical Society, is the author of an article "The Work of the Conference of State Presidents" which appeared in the *Bulletin of the Association of American Physicians and Surgeons* for February, 1947.

\* \* \*

"Chronic Liver Impairment" is an original article appearing in the March 29 issue of *The Journal of the American Medical Association* by John D. Mateer, M.D., James I. Baltz, M.D., Hugh H. Steele, M.D., Stephen W. Brouwer, M.D., and James R. Colvert, M.D., all of Detroit.

\* \* \*

Frank VanSchoick, M.D., Jackson, Chairman of the MSMS Child Welfare Committee, was official representative of the Michigan State Medical Society at the State Meeting on Polio, sponsored by the National Foundation for Infantile Paralysis and held in Lansing on May 14.

\* \* \*

President Wm. A. Hyland, M.D., Grand Rapids, addressed the Medical and Legislative Committees of the American College of Surgeons in Chicago on March 6. His subject was "A Program of Co-operation in Cancer Control Between the State Medical Society and the American Cancer Society."

\* \* \*

Olin West, M.D., President-elect of the American Medical Association, resigned in April, because of ill health. Edward L. Bortz, M.D., Philadelphia, Vice-

## WHAT'S WHAT

President, will succeed Dr. West, and will be inaugurated as President at the Annual Session in Atlantic City in June.

\* \* \*

"*The Present and Future Role of the General Practitioner in Medicine*" was the subject of an address by Wm. H. Marshall, M.D., Flint, at the regular general staff meeting at Hurley Hospital on April 18. The discussants were J. T. Connell, M.D., and Walter H. Winchester, M.D., of Flint.

\* \* \*

*The Shoe, Convalescent, Orthopedic*, on which the Army opened procurement in January 1947, had its basic design contributed by Mr. Nathan Hack, Detroit shoeman, according to a press release from Colonel H. W. Bobrink, Commanding Officer of the Boston Quartermaster Depot.

\* \* \*

The Jackson County Medical Society developed a three-page questionnaire listing "Vital Statistics" on each of its members, for the archives of the Society. For information and a sample of this very interesting blank, write Horace Wray Porter, M.D., Secretary, 505 Wildwood, Jackson.

\* \* \*

*Medicine and Industrial Research.*—Mr. C. F. Kettering's paper on the above subject which was published in this JOURNAL in August, 1946, has been translated into Spanish and published in *Revista de Radiologia y Fisioterapia*, Enero-Febrero de 1947. We are pleased to receive a copy.

\* \* \*

The Florida Medical Association has selected Ernest R. Gibson as Director of its newly created Public Relations Bureau. Mr. Gibson, who has lived in Florida two years, is a native of Ohio. While in the Navy, he served as Public Information Officer to the Commander of the Naval Air Training Base, Pensacola.

\* \* \*

Senate Bill 215 in the Michigan Legislature would authorize osteopaths to make examinations for the commitment of the insane under the hospital act for mentally diseased persons. This is a further extension of the osteopaths into the field of medicine. Each little step like this leads to complete practice of medicine.

\* \* \*

*New Dates:* Examination by the Michigan State Board of Registration in Medicine will be held at the Auditorium of the College of Medicine, Wayne University, Detroit, on Monday, Tuesday and Wednesday, June 9, 10, and 11, 1947. For further information write the State Board of Registration in Medicine, 202 Hollister Building, Lansing, Michigan.

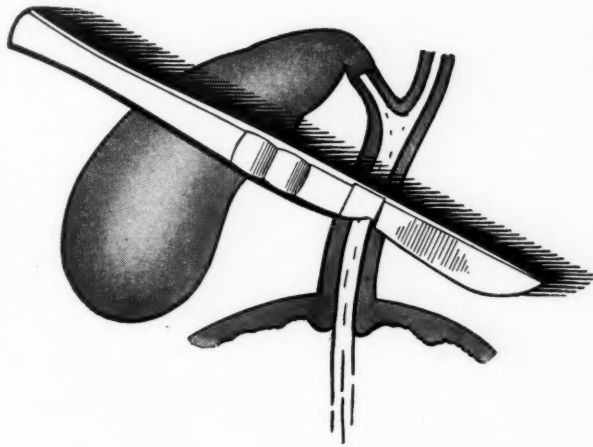
\* \* \*

*Woman's Auxiliary.*—Haddon Hall will be the headquarters for the Annual Meeting of the Woman's Auxiliary to the American Medical Association, which will be held in Atlantic City, New Jersey, June 9-13, 1947.

Requests for reservations should be sent immediately to Dr. Robert A. Bradley, Chairman, Subcommittee on Hotels, 16 Central Pier, Atlantic City, New Jersey.

MAY, 1947

Say you saw it in the *Journal of the Michigan State Medical Society*



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*The Upper Peninsula Medical Society* will hold its Annual Session at the Four Seasons Club, Pembine, Wisconsin, on Friday-Saturday, June 27-28, 1947. All members of the Michigan State Medical Society are cordially invited to attend. For program and reservations at the Club, write W. S. Jones, M.D., Menominee, Michigan.

\* \* \*

*The American Medical Golfing Association* will hold its 31st Tournament at Atlantic City, New Jersey on Monday, June 9. Linwood Country Club and the Atlantic City Country Club both have been reserved for the 250 or more Fellows, who are anticipated will attend. Application blanks may be secured from AMGA Secretary Bill Burns, 2014 Olds Tower, Lansing 8.

\* \* \*

*The Upper Peninsula Medical Society Annual Session*, to be held at the Four Seasons Club, Pembine, Wisconsin, Friday, Saturday, June 27-28, 1947, will present on its program F. A. Collier, M.D., Ann Arbor; C. G. Johnston, M.D., Detroit; Hardy A. Kemp, M.D., Detroit; M. Edward Davis, M.D., Chicago; Jack Gale, M.D., Madison, Wisconsin, and Robert Burns, M.D., Madison, Wisconsin.

\* \* \*

*Michigan Physicians Committee*, a branch of the National Physicians Committee for the Extension of Medical Service, has the following officers: C. E. Umphrey, M.D., Detroit, Chairman; Wm. M. LeFevre, M.D., Muskegon, F. J. O'Donnell, M.D., Alpena, W. H. Huron, M.D., Iron Mountain, Vice-Chairmen; E. R. Witwer, M.D., Detroit, Secretary-Treasurer. The address of the Secretary is 3829 Brush St., Detroit 1.

\* \* \*

*S. 140 and S. 712* are an effort to place the Federal Security Agency in the President's cabinet, with the medical head of the health services subordinate to the social worker, or other non-medical individual. Those in general who advocated the Wagner-Murray-Dingell type of legislation are very active in testifying for these two bills. The best interests of the Medical profession, we believe, are in S. 545.

\* \* \*

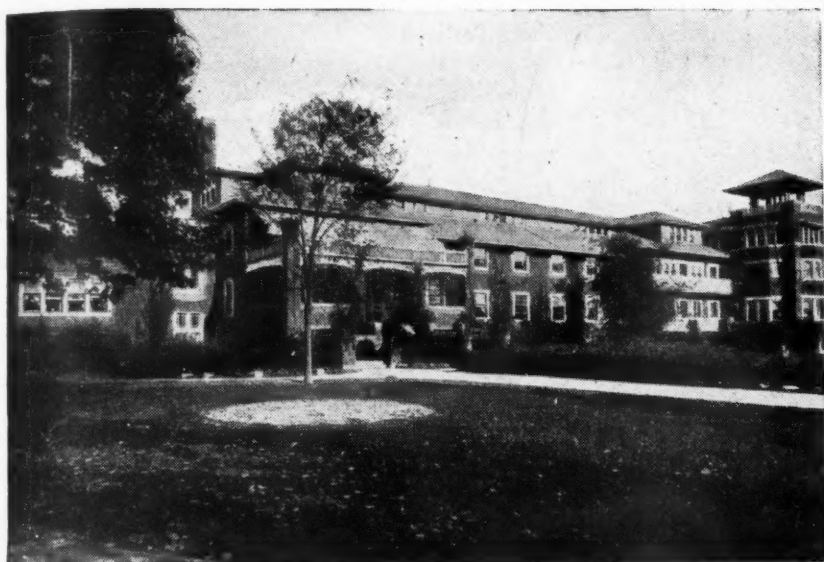
*Wm. A. Hyland, M.D.*, Grand Rapids, President of the Michigan State Medical Society, addressed the New York Academy of Medicine on April 4 on the subject "The Michigan Health Plan." A spirited question and answer period, in which Senator H. Alexander Smith of New Jersey joined, resulted from Dr. Hyland's brief presentation of medico-economic activities in Michigan, which included a progress report on Michigan Medical Service.

\* \* \*

*Under the provisions of the Narcotics Drugs Import and Export Act*, it is unlawful for a physician to carry narcotic drugs in his medical bag back and forth between the United States and Mexico and between the United States and Canada. Narcotic drugs found in the possession of a physician upon returning to the United States are seized and forfeited. Because of lack of knowledge of the law many physicians are caused embarrassment

(Continued on Page 592)





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offering all forms of treatment, including electric shock.

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(Continued from Page 590)

and inconvenience when travelling between this country and Mexico or Canada. This information is published in order that physicians may be correctly informed with reference to this provision of the Federal law.

\* \* \*

The AMA Council on Pharmacy and Chemistry has expanded its activities with a project operated by the Therapeutic Trials Committee which will be charged with the responsibility of aiding doctors of medicine with their research studies through a greater exchange of information. The value of planning co-operative research and disseminating the proper information is unquestioned. Through these means the medical profession will have at its command added facilities for supplying it with necessary information quickly and accurately.

\* \* \*

The Genesee County Medical Society's Second Annual Cancer Day was a most successful postgraduate clinic, held at Flint on March 19. Speakers included Cornelius P. Rhoads, M.D., New York, A. C. Furstenberg, M.D., Ann Arbor, G. Gavin Miller, M.D., Montreal, George N. Papanicolaou, M.D., New York, David Steele, M.D., Cleveland, and Charles F. Kettering, Sc.D. of Detroit. W. Z. Rundles, M.D., President of the Genesee County Medical Society was toastmaster at the banquet in the Durant Hotel.

\* \* \*

Harefuah, The Journal of the Palestine Jewish Medical Association, has been received. This is the foreign edition, published in Tel-Aviv, Palestine. There are four articles, "Sterility in Women," "Remittent Rural Fever," "Huet-Pelger Anomaly of the Nuclei of the Leukocytes in a Jewish Family in Palestine," and "Dermatitis Among Workers Employed in the Citrus By-Product Industry." These are all printed in English. Anyone who wishes may join the society by addressing an application to the Association 9, Yavneh St., Tel-Aviv.

\* \* \*

#### Council and Committee Meetings

Rural Health Committee, April 9, Lansing  
Uniform Fee Schedule for Governmental Agencies Committee, April 10, Detroit  
Legislative Committee, April 10, Lansing  
Executive Committee of The Council, April 16, Detroit  
Mental Hygiene Committee, April 17, Detroit  
Cancer Control Committee, April 18, Detroit  
Executive Committee of The Council, May 13, Grand Rapids

\* \* \*

*Deduction for Medical Expense.*—Mr. Morrison of Louisiana introduced in the House of Representatives a Bill, H. R. 2526, on March 12, 1947, which repeals the limit on deductions from income tax statements for medical and health services. The present limit is 5 per cent of the gross income. If this new bill passes it will make a real problem in bookkeeping for all doctors, hospitals, dentists and others. At the end of the

(Continued on Page 594)

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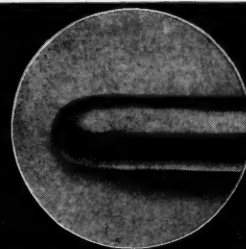
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(Continued from Page 592)

year all patients will be calling to know the total they paid each health service purveyor. Now it is necessary only when the amount is considerable.

\* \* \*

Harry A. Pearce, M.D., Detroit and Alfred L. Chaput, D.D.S. of Royal Oak, recently returned from an interesting six weeks in Central America during which they visited the rugged highlands of San Pedro Soloma, Huehuetenango (pronounced Wa-wa-tenango), Guatemala. The six-day stay at Soloma represented a week of hard work for the two doctors who were prevailed upon by the local padre to create a "clinic" for the undernourished, primitive Indian people, wards of the mission. Doctors Pearce and Chaput were among the first white people ever to visit San Pedro Soloma.

\* \* \*

College of American Pathologists, Inc.—Dr. Melbourne G. Westmoreland, Hospital Inspector, Council on Medical Education and Hospitals, is leaving A.M.A. the middle of April to become Executive Secretary of the newly organized College of American Pathologists, Inc. Headquarters will be in Chicago. Dr. F. W. Hartman, Pathologist, Henry Ford Hospital, Detroit, is President; Dr. Tracy B. Mallory of Boston, Secretary-Treasurer; Dr. Granville Bennett, University of Illinois, Vice-President and Dr. J. J. Moore of Chicago, a member of the Board of Governors.

\* \* \*

"The National Conference of County Society Officers to be held at Atlantic City on Sunday, June 8, should serve a great purpose in informing the individual doctor what the American Medical Association is able to do for him as there are only a few states which hold an annual County Secretaries Conference such as is held in Michigan."—D. Bruce Wiley, M.D., Utica, Michigan, Michigan Chairman for the National Conference of County Society Officers.

Dr. Wiley invites all officers of Michigan County Medical Societies to attend the Conference scheduled for June 8.

\* \* \*

Changing Age Averages.—According to U. S. Census figures, and reliable estimates with respect to the future, the following figures represent the proportion of our population forty-five and sixty-five years and over at various dates:

Year	45	65
1860	13.1%	2.7%
1880	16.0%	3.4%
1900	17.8%	4.1%
1920	20.8%	4.7%
1940	26.5%	6.8%
1960	33.3%	10.0%
1980	40.3%	14.4%

\* \* \*

U. S. Senator Robert A. Taft and Major General Paul R. Hawley of the Veterans Bureau have accepted invitations to speak at the Conference of Presidents and

(Continued on Page 596)

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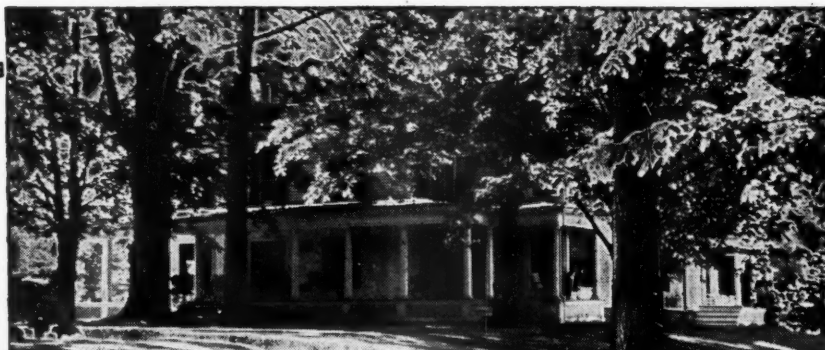
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## WHAT'S WHAT

(Continued from Page 594)

Other Officers of State Medical Associations, scheduled for the Ritz-Carlton Hotel, Atlantic City, N. J., on Sunday, June 8, 1:30 p.m. (the day preceding the opening of the Centennial Session of the American Medical Association).

L. Howard Schriever, M.D., Cincinnati, President-elect of the Conference of Presidents, will address the Conference on "A Medical Profession's Program to Improve Medical Care."

All officers and members of state medical associations are cordially invited to attend the annual meeting of the Conference of Presidents. No registration fee.

\* \* \*

**Wayne University Diplomas Available to Older Graduates.**—Any graduate of the antecedent colleges of Wayne University who wishes to obtain a Wayne University diploma may now secure an application for such a diploma in the Alumni Office. The fee for the new diploma is three dollars (\$3.00).

Degree holders of the Detroit College of Medicine and Surgery, Detroit Teachers College, College of the City of Detroit, Colleges of the City of Detroit, Detroit College of Pharmacy, and Detroit City Law School are eligible to request the Wayne diplomas; it is not necessary to turn in the original copy.

Many graduates have expressed regret that, although they are, in fact, Wayne University alumni, their diplomas do not so identify them.

The Kent County Medical Society has authorized its Program Committee to submit a plan to the resident staff of the three Grand Rapids hospitals whereby all interns and residents are invited to prepare papers of scientific or clinical interest on a subject of their individual choosing. The three papers most suitable for presentation will be heard by the Kent County Medical Society at a meeting to be known as "Residents' Night" annually in November.

Cash awards to the three successful contestants will be made, and the papers will be submitted for publication.

Congratulations, Kent County Medical Society, and may your worthwhile plan in postgraduate endeavor meet with success.

\* \* \*

**Industrial Health Speakers Roster.**—The Committee on Professional Relations of the Council on Industrial Health of the AMA is setting up a roster of speakers containing names of doctors who can discuss the benefits of good industrial health services with groups of employees and the public. Some time ago the chairmen of state committees on industrial health were asked to suggest names of doctors to formulate this roster, and to date approximately 150 names have been received. The Council on Industrial Health will provide the material and guidance for the speakers.

Clarence D. Selby, M.D., Detroit, Chairman; Wm.

(Continued on Page 598)



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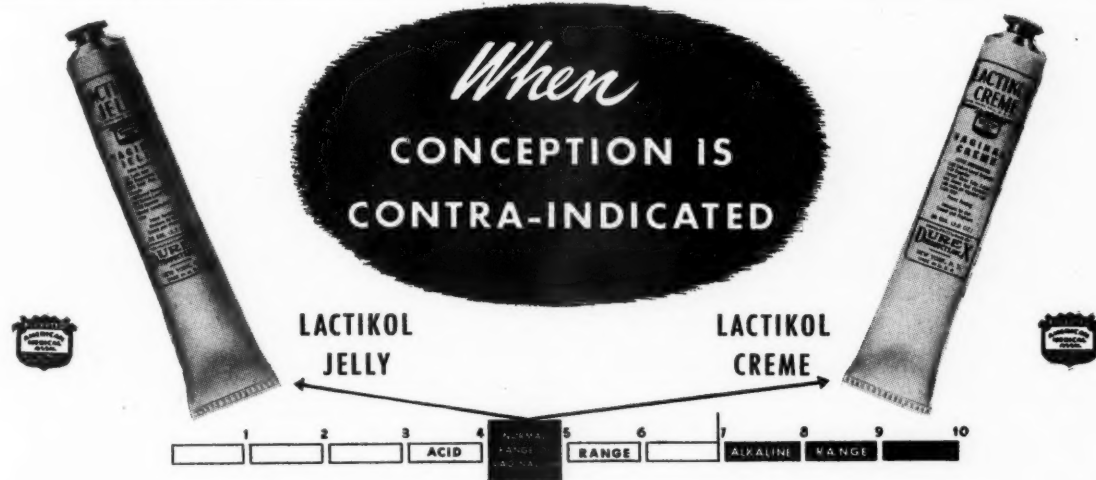
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## WHAT'S WHAT

(Continued from Page 596)

A. Sawyer, M.D., New York, and Anthony J. Lanza, M.D., New York, compose the Committee on Professional Relations. Dr. Harold R. Hennessey, Chicago, is executive officer.

\* \* \*

**Displaced Persons.**—As a result of the war, and two years after its end there are 850,000 displaced persons in Europe living in detention camps. Of these 4,057 are trained nurses and 1,135 experienced hospital attendants. With our shortage of nurses and hospital attendants the Chairman of the Citizens Committee on Displaced Persons believes "it is a crime to allow these persons to literally rot in these camps."

H.R. 2910, sponsored by Rep. William G. Stratton, Jr., R. of Illinois, would allow an excess of immigration up to 100,000 each year for four years applicable to these displaced persons. This would still be under what the normal legal immigration for the past sixteen years would have allowed from these countries. 2,614,273 visas were available and fewer than 600,000 were used.

These persons are said to be 80 per cent Christian and 20 per cent Jews.

\* \* \*

**"Doctor of Medicine"**—Radio Station CKLW—Fridays at 12:45 P.M. Prepared by the Michigan State Medical Society and sponsored as a public service by the Hack Shoe Company.

January 31—Edward D. Spaulding, M.D.—The Heart and Its Disorders

February 7—D. C. Beaver, M.D.—The Pathologist and The Patient

February 14—Francis F. MacMillan, M.D.—Common Sense Advice on Fractures

February 21—J. J. Lightbody, M.D.—Rheumatism and Arthritis

February 28—Charles S. Kennedy, M.D.—Gall Stones

March 7—W. S. Gonne, M.D.—Your Most Precious Possession—Your Eyes

March 14—Eugene A. Osius, M.D.—Varicose Veins

March 21—Ruth M. Kraft, M.D.—Children's Feet and Shoes

March 28—Harold C. Mack, M.D.—Change of Life

April 4—Clarence E. Umphrey, M.D.—Public Enemy Number One

\* \* \*

Michigan has 5,103 practitioners of medicine in all ages, according to the Medical Mailing Service of Chicago. Those under 69 years of age total 4,902. Those in general practice total 2,860 of which 2,575 are under 69 years of age.

The breakdown of medical specialists in the United States, according to the same source, is as follows:

Allergists .....	349
Ear, Nose and Throat.....	1,791
Anesthetists .....	769
Bacteriologists .....	98

(Continued on Page 600)

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(Continued from Page 598)

Cardiologists .....	542
Clinical Pathologists .....	355
Dermatologists .....	1,354
Gastroenterologists .....	328
Gynecologists .....	856
Industrial Practice .....	1,708
Internists .....	5,712
Neurologists .....	155
Neuro-Psychiatrists .....	1,560
Neurological Surgeons .....	180
Eye, Ear, Nose and Throat.....	4,141
Obstetricians .....	2,138
Obstetricians and Gynecologists .....	4,135
Ophthalmologists .....	1,970
Orthopedic Surgeons .....	1,495
Pathologists .....	770
Plastic Surgeons .....	130
Pediatricians .....	4,208
Proctologists .....	723
Psychiatrists .....	1,033
Public Health .....	1,388
Roentgenologists .....	2,164
Surgeons .....	14,182
Tuberculosis .....	1,078
Urologists .....	2,232

Total: .....57,544

\* \* \*

**MICHIGAN'S DEPARTMENT  
OF HEALTH**

(Continued from Page 576)

**ENTERS PRIVATE PRACTICE**

George A. Sherman, M.D., Director of the Bureau of Tuberculosis Control, Michigan Department of Health, resigned effective March 1, to enter the practice of internal medicine in Lansing. Dr. Sherman, who came to the Department in February, 1941, is continuing to serve as director of the Bureau until his successor can be found.

**INCIDENCE OF COMMUNICABLE DISEASE**

Disease	March 1947	March 1946	7-year median
Diphtheria	22	42	25
Gonorrhea	884	1,083	813
Lobar pneumonia	166	75	279
Measles	263	13,527	3,306
Meningococcic meningitis	14	20	20
Pertussis	1,003	466	565
Poliomyelitis	3	2	1
Scarlet fever	769	689	1,326
Syphilis	1,412	1,478	1,373
Tuberculosis	614	438	489
Typhoid fever	4	5	5
Undulant fever	18	10	9
Smallpox	0	0	1

*The Eye Bank for Sight Restoration* has been in operation for about a year. There was an article by Derrick Vail, M.D., Editor of the *American Journal of Ophthalmology* in June, 1946, on this subject. The effort is to collect healthy corneal tissue for transplanting to the eyes of persons who have lost their sight through corneal defects. Also the object is to train surgeons in the technique of this delicate operation. The public response to this stimulating and dramatic cause has been and continues to be strong and active. As more funds become available the influence set at work by the activities of the Eye Bank are certain to spread and result in much good to the cause of human welfare.

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*Acknowledgment of all books received will be made in this column and this will be deemed by us as a full compensation of those sending them. A selection will be made for review, as expedient.*

**CARDIOVASCULAR DISEASES** By David Scherf, M.D., F.A.C.P., Associate Professor of Medicine, New York Medical College, Flower and Fifth Avenue Hospitals; and Linn J. Boyd, M.D., F.A.C.P., Associate Professor of Medicine, New York Medical College, Flower and Fifth Avenue Hospitals. 56 Illustrations. Philadelphia: J. P. Lippincott Co., 1947. Price \$10.00.

This text is one of the most important additions to the Medical Man's Library in the past few years. Former editions, which were favorably received and translated into seven different languages, have been completely rewritten, and much new, usable and authoritative information has been added.

Beginning with a chapter on dyspnea and ending with one on therapy, many previously omitted or lightly touched subjects are here covered in detail. Topics such as rheumatic fever, arteriovenous anastomosis, irradiation of autonomic reflexes, the cardiac neurosis and neuro-circulatory asthenia, peripheral vascular diseases, hypertension, anginal pain and its differential diagnosis, the heart in endocrine disturbances, and cardiac disease in pregnancy are lucidly discussed.

The widespread incidence of myocarditis is again stressed and emphasized. The chapter on subacute bacterial endocarditis contains a detailed account of the current use of penicillin in this previous inevitably fatal condition. Another valuable addition is the attention

given to roentgenology of the cardiovascular system in connection with the various subjects.

A few electrocardiograms are reproduced, but a detailed discussion is omitted as the authors' companion book on electrocardiography amply covers this field.

This authoritative and detailed description of the cardiovascular disease can be recommended as a valuable addition to the physician's library and will be of marked aid in his practice.

**RADIOLOGY FOR MEDICAL STUDENTS.** By Fred Jenner Hodges, M.D., Professor and Chairman, Department of Roentgenology, University of Michigan; Isadore Lampe, M.D., Associate Professor, Department of Roentgenology, University of Michigan; and John Floyd Holt, M.D., Assistant Professor, Department of Roentgenology, University of Michigan. Chicago: The Year Book Publishers, 1947. Price \$6.75.

Here is a handbook on radiology for students, entirely authored by our own University of Michigan teachers. It is clear, not controversial, and gives the essentials in the study of roentgenology for the medical student. It is not a complete text and does not intend to be, but is a very well-prepared guide for the undergraduate and the general man in medical practice. We are pleased to recommend this book.

**MODERN DERMATOLOGY AND SYPHILOLOGY.** By S. William Becker, M.D., Clinical Professor of Dermatology, University of Chicago, and Maximilian E. Obermayer, M.D., Clinical Professor and Chairman of the Department of Dermatology, University of Southern California. Second Edition. 461 Illustrations in text. 37 full-color plates. Philadelphia: J. P. Lippincott Company, 1947. Price \$18.00.

This is a full sized textbook of over a thousand pages filled with the most complete and up-to-date information on the subject of dermatology. It is complete in detail

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and descriptions and contains pages of references for the student who wishes to pursue research. The illustrations are excellent and present the subject of dermatology through the only understandable method. Early in the book is a page of drawings giving the sixteen different kinds of skin lesions and their names, so references in the book will be understood. A long chapter is devoted to drug dermatoses, and another to physical dermatoses. Diseases due to filterable virus are given prominent space, and of course syphilis is extensively covered, including diagnosis and treatment. This is a most satisfactory volume for the student and the practitioner.

**PROGRESS IN GYNECOLOGY.** Edited by Joe V. Meigs, M.D., Clinical Professor of Gynecology, Harvard Medical School; Chief of the Vincent Memorial Hospital, the Gynecological Service of the Massachusetts General Hospital; Surgeon, Pondville Hospital; Gynecologist, Palmer Memorial Hospital, and Somers H. Sturgis, M.D., Chief, The Vincent Memorial Hospital Laboratory; Assistant Surgeon, Massachusetts General Hospital. New York: Grune & Stratton, 1946. Price \$7.50.

This is a composite of short papers from seventy-one writers on the subject of Gynecology and its kindred branches. Everything new has been selected and included. The individual papers are reports of careful studies and research, brought together for the benefit of the practicing physician. It is impossible to point out specific subjects that will interest the reader, but the latest information on sterility, operative treatment of prolapsus uteri, et cetera, is here. This is a very interesting and instructive volume.

**FUNDAMENTALS OF CLINICAL NEUROLOGY.** By H. Houston Merritt, M.D., Professor of Clinical Neurology, College of Physicians and Surgeons, Columbia University, Chief of Division of Neuropsychiatry, The Montefiore Hospital; Fred A. Mettler,

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M.D., Ph.D., Associate Professor of Anatomy, College of Physicians and Surgeons, Columbia University; and Tracy Jackson Putnam, M.D., Professor of Neurology and Neurological Surgery, College of Physicians and Surgeons, Columbia University. Philadelphia: The Blakiston Company, 1947. Price \$6.00.

The text of this book is divided into two parts. Examination of the nervous system deals with the examination of the cranial nerves, the motor system and the sensory system. Most of the book is devoted to anatomic diagnosis. This part is technical, tracing the anatomic causes of disease, the nerve lesions, the spinal cord lesions, tracts, and relations. Many pictures and diagrams are used. Cortical changes and areas and their effect on the health of the body are outlined. A handy book for fundamental studies in neurology.

PHYSICAL MEDICINE IN GENERAL PRACTICE. Edited by Arthur L. Watkins, M.D., Associate in Medicine, Harvard Medical School; Chief of Physical Medicine, Massachusetts General Hospital, etc. Philadelphia: J. B. Lippincott Company, 1946. Price \$5.00.

Fourteen authors have contributed articles to this symposium, presenting the history and development of physical medicine, factors to be considered in prescribing physical methods; principles in treating dermatological conditions; minor injuries, fractures, and orthopedic disabilities. The author himself describes the uses of physical medicine in neurology. Physical and occupational therapy are well known in psychiatry, rehabilitation and employment. The uses of cold in surgery are well presented. All in all, this is a very interesting and instructive book.

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## GYNECOLOGICAL AND OBSTETRICAL PROBLEMS OF THE INDUSTRIAL PHYSICIAN

(Continued from Page 558)

his health maintenance program. His ultimate objective is safe placement at work, the reduction of sick absenteeism, and the correction of working conditions that may result in disability or aggravation of an existing disease.

It can be definitely stated that such a program cannot be developed without the co-operation of the physicians in private practice. Further, the extent to which these programs are successful depends directly upon the amount of understanding of each others problems.

That this can be done ethically and scientifically has been proved repeatedly. The best interests of the medical profession, the employer, the employee and the community at large are served when the responsibility of such a relationship is clearly understood.

## NATIONAL HEALTH ACT OF 1947

(Continued from Page 506)

### VI. Further Research and Training (Title IX)

This portion creates an institute of Dental Research as a division of the National Institute of Health. The Institute shall have sufficient funds for its operation, and \$2,000,000 is appropriated for new construction.

### VII. Miscellaneous

There are outlined in Title III various legal technicalities, including changes in numbering of the various portions of previous Acts amended by this Bill. Various references to administrative provisions appear in Sections 3, 105-109, 201-202, 715-718.

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Roger E. Heering, Ohio Director of Health, submitted his resignation to Governor Herbert after the Ohio Legislature failed to appropriate more state funds for the Department so it would not be forced to use so much federal money for the operation of the Department. Between \$700,000 and \$800,000 of federal funds are being spent annually; of the 235 employes of Department's offices in Columbus, Ohio, 152 are being paid from federal funds, including the salaries of five division chiefs.

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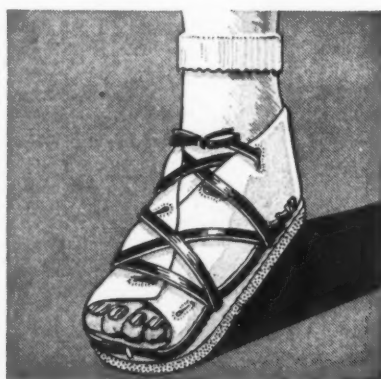


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## DETROIT PHYSIOLOGICAL SOCIETY

(Continued from Page 572)

testine appears to be increased and the amplitude of contraction is greater when the strip is immersed in a solution of the protein substance, previously dialyzed against Tyrode's solution.

### Effect of Methyl Testosterone on Calcium Metabolism in Growing Boys

Joseph A. Johnston, M.D., Pediatrician-in-Chief,  
Henry Ford Hospital, Detroit, Michigan.

Studies were made of the nitrogen and calcium balances of five boys aged seven, ten, ten, fourteen and fifteen years. Striking increases in the storage of nitrogen were noted but the calcium balance was consistently reduced, the losses being referable to an increase in stool calcium. The urinary excretions fell.

In interpreting an observation such as this, it should again be pointed out that among the many items conditioning the action of a hormone, one outstanding one will be whether or not the material administered supplies a defect or creates an

excess; presumably it is the latter we were measuring. It is probable too that a different effect would result from the administration of androgens to the female; the subjects were all male. Finally, as in the case of divergent reports on the effect of estrogens on calcium retention, the age of the subject would be expected to play a role and it would not be surprising if quite different effects followed the use of this material in the aged.

## NUTRITION AND INFECTION

(Continued from Page 565)

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## BRIEF HISTORICAL NOTES ON MEAD'S CEREAL, PABLUM AND PABENA

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**H**AND in hand with pediatric progress, the introduction of Mead's Cereal in 1930 marked a new concept in the function of cereals in the child's dietary. For 150 years before that, since the days of "pap" and "panada," there had been no noteworthy improvement in the nutritive quality of cereals for infant feeding. Cereals were fed principally for their carbohydrate content.

The formula of Mead's Cereal was designed to supplement the baby's diet in minerals and vitamins, especially iron and thiamine. How well it has succeeded in these functions may be seen from two examples:

- (1) As little as one-sixth ounce of Mead's Cereal\* supplies over 50% of the iron and 20% of the thiamine minimum requirements of the 3-months-old infant.
- (2) One-half ounce of Mead's Cereal furnishes all of the iron and 60% of the thiamine minimum requirements of the 6-months-old baby.

That the medical profession has recognized the importance of this contribution is indicated by the fact that cereal is now routinely included in the infant's diet as

early as the third or fourth month instead of at the sixth to twelfth month as was the custom only a decade or two ago.

In 1933 Mead Johnson & Company went a step further, improving the Mead's Cereal mixture by a special process of cooking, which rendered it easily tolerated by the infant and at the same time did away with the need for prolonged cereal cooking in the home. The result is Pablum, an original product which offers all of the nutritional qualities of Mead's Cereal, plus the convenience of thorough scientific cooking.

During the last twelve years, these products have been used in a great deal of clinical investigation of various aspects of nutrition, which have been reported in the scientific literature.

Many physicians recognize the pioneer efforts on the part of Mead Johnson & Company by specifying Mead's Cereal and PABLUM—and also the new Pablum-like oatmeal cereal known as PABENA.

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\*Pablum, the precooked form of Mead's Cereal, has practically the same composition: wheatmeal (farina), oatmeal, cornmeal, wheat embryo, beef bone, brewers yeast, alfalfa leaf, sodium chloride, and reduced iron.  
Mead Johnson & Co., Evansville 21, Indiana, U. S. A.